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FOREWORD

It is a distinct honor for the University of Arkansas Medical Center to be signalled to carry the responsibility for the scientific tone of this issue of *The American Surgeon*. It has been in some part a tradition for the Dean of the School to review the history of the School in order to set the stage and scenery of the environment from which the following papers arise. Even though the University of Arkansas School of Medicine is 78 years of age and has a rich history, these papers are being written more under an anticipation of the future rather than from what has gone before.

In April of 1957 a new University Medical Center was dedicated. It was dedicated to the people of Arkansas and to those who will teach and explore the medical sciences. Now for the first time the School of Medicine is in a position to be most effective in its role as an institution of higher learning. With the construction of the new Center the State gave recognition to the importance of a Medical Center as a factor potentiating the development of the State and the future of Arkansas.

The credit for these developments goes to many; the responsibility for charting the future rests with a few. To this end the students and faculty will play a most important role. Of course, this challenge is not unique to this School of Medicine but after many years of waiting the new mandate is most welcomed at the University of Arkansas. The school is now actively involved in the recruitment of a dynamic faculty—men who are devoted teachers and inspired investigators.

A primary step was taken in July of 1956 with the establishment of a full-time staff appointment system. This for the first time provides for a basic teaching staff which will devote its full efforts to teaching and research. Of course, there remains a very important and dedicated volunteer faculty in the clinical field which has long given valuable assistance to our teaching program. They give depth to the clinical departments and to the various specialties which could not possibly be covered through direct state appropriation. It is in large part due to the ideals and persistence of these men that the new Medical Center has become a reality. The University is most grateful to them for their fine support over these formative years.

The University Hospital has a capacity of 450 beds but only about 300 have been activated so far. The great majority of the patients are medically indigent; however, any patient can be referred for care. All patients seen at the Center are part of the teaching program and the variety of illnesses seen are almost unlimited.

During the next two years additional research facilities will be built. This construction will round out present facilities and provide the University Medical Center with a potential as great as that of any institution in the country for the advancement of education and research in the medical sciences.

With the new facilities and the active recruitment of a full-time staff, the University of Arkansas Medical Center is taking on a new look—an appearance which will spell out excellence in education, a dedication to the acquisition of new knowledge and a devotion to serving the people of Arkansas. Thus, it can be seen that the University Medical Center has been built with vision and imagination for the future.

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CAROTID BODY TUMORS: A REPORT OF THREE CASES

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The carotid body and the neoplasms which arise in it have engaged the interest of anatomists, embryologists, physiologists, pathologists, internists, surgeons, otolaryngologists and others of this and many other countries. The extent of interest is out of proportion to the number of reported cases which are only about 300 since the original description by Marchand in 1891. Information is being accumulated but the fact remains that much is unclear.

There is uncertainty as to the function of the carotid body itself. There is just beginning to be some understanding that there is other similar tissue in the chest and in other locations in the neck. Presumably this tissue has the same function as the carotid body and harbors similar tumors. The difficulties involved in working out the embryology of these various normal organs are obvious. There is a variety of opinion as to the frequency and the degree of malignancy. There is room for error in the clinical recognition of the tumors. Clinicians do not agree as to the advisability of removing the tumors. The problems and risks attending the surgical removal are considerable. Details of surgical technic are important and not universally known.

The purpose of this article is more simple than to attempt a review of all of these problems. It is contemplated only to remark upon a few points which may be of special interest to the clinical surgeon. In addition we wish to report briefly 3 cases and to add a few facts concerning the handling of patients having these tumors.

We will omit a review of the classical features of carotid body tumors which are well described in all standard textbooks and in many articles such as one by Warren.⁴

An article by Lattes² is helpful in arriving at some idea of the general function of normal carotid body tissue. In his article he reports 4 interesting cases of tumors of the carotid body type arising in unusual locations. In the discussion and comment he brings some order to the confused problem of accurately placing the carotid body tumors in relation to the whole group. At the risk of over simplifying his excellent discussion let it be said that the paragangliomas may be divided into 2 large groups, namely, those which take the chromaffin stain and those which do not. In the chromaffin series which are epinephrine producing tumors there are the pheochromocytoma arising from the adrenal medulla and those associated with the sympathetic ganglia and the celiac and pelvic plexus. The carotid body tumor is one of the nonchromaffin, nonepinephrine producing series and is grouped with the glomus jugulare (which tumors are approached surgically through the mastoid region) and the aortic arch bodies or glomus

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aorticum. The function of these organs is that of a chemoreceptor having the ability to detect changes in pH and CO₂. Chemoreceptors undoubtedly have other complex chemical functions as yet unrecognized. Other more distantly related tumors of this general group are those involving the sensory nerve endings of large blood vessel walls as well as the neuromyoarterial glomus at the finger tips and under the nails.

CASE REPORTS

Brief resumes of 3 cases are as follows.

Case 1. Mr. J. E. O., aged 46, St. Vincent Infirmary: This patient went to his physician because of a tender mass in the left upper portion of the neck. The tumor was explored, biopsy obtained and diagnosed as carotid body tumor before he was referred to us. Unfortunately there was infection in the wound. This prevented definitive operation for 3 months.

The operative dissection was complicated by the previous infection. The gland, which weighed 20 grams after removal, completely encased the bifurcation of the carotid artery and it was necessary to sacrifice the external carotid at the bifurcation in order to remove it satisfactorily. The common carotid and the internal carotid were intact at the end of the operation. Postoperatively the patient's condition was excellent for 6 hours and there was good movement of all extremities. At the end of that time he developed weakness in the right upper extremity which later involved the left side of the face to some extent and the right lower extremity to a slight extent. Stellate blocks were utilized and anticoagulants were begun. His general condition was never serious but the paralysis improved only slowly and over a period of months. He had no speech difficulties although he was right handed.

Follow-up 4 years later showed no suggestion of recurrence. The neurologic features have long since cleared up entirely in the face and in the right lower extremity although there are minor residuals in the fine movements of the right hand.

Case 2. Mrs. H. D., aged 35, St. Vincent Infirmary: This patient had noticed a mass at the angle of the mandible on the right side for 5 years. It had increased in size during the past 2 years. She began to have dizzy and fainting spells during the past year and on one recent occasion fell to the floor because of dizziness.

Operative removal of this tumor was accomplished without injury or division of any portions of the carotid artery or its bifurcation. The gland weighed 15 grams. We found it easiest to begin the removal from the common carotid artery and to complete the removal here and on the external carotid before accomplishing the more crucial removal from the internal carotid. Heparin was begun 2 hours following operation and continued for several days. This patient had no complications whatsoever and has remained well with no recurrence during the 3 years since operation.

Case 3. Mrs. B. N., aged 37, St. Vincent Infirmary: She had noticed a mass in the right side of the neck for 1 year. There was a disagreeable sensation of pulsation and tenderness. Preoperatively we had not really expected this to be a carotid body tumor because of its rather free mobility.

The operative procedure was uneventful although made more difficult because she was of excessive weight and had an extremely short neck. It was found more expedient to remove the tumor in this patient from the more laterally placed internal carotid artery before removing it from the common carotid and from the external carotid. The external carotid was sacrificed leaving an ample bifurcation with good pulsation. Heparin was given postoperatively beginning approximately 2 hours after surgery and continuing for several days. There was no postoperative difficulty and the patient has had a good convalescence and follow-up to this date some 18 months since operation. This gland weighed 10 grams.

Surgical removal of these tumors occupied from 4 to 5 hours of time in each case. Ample exposure, tedious hemostasis and the placing of a loose tape about the common carotid is advisable before any attempt is made to remove the tumor from the vessels. Our experience in removing the tumors from the vessel is similar to that well described by Morfit, Swan and associates.³ A line of cleavage can be nicely established either just outside the adventitia or more commonly to include the adventitia in its removal with the tumor. The tumor can sometimes be removed without cutting into it but by freeing up an edge and separating it from that point onward. In other patients it seems necessary to divide through the tumor down to and including a portion of the adventitia. There is of course no harm in sacrificing the external carotid artery although the bifurcation and the internal carotid must be saved or repaired. We have had no necessity for the use of a venous transplant, homologous arterial transplant, or the use of a foreign body vessel. Any of these, however, would be preferable to a sacrifice of the carotid circulation and must be utilized if that circulation has been interrupted.

After the experience encountered in case number 1 in which this patient had good circulation for 6 hours and later developed what was certainly a cerebral thrombosis, we have favored the postoperative utilization of heparin. Anti-coagulants are not universally recommended in this situation but it is our experience that if they are begun some 2 hours after operation that the hazards of a hematoma in the wound are not as great as the hazard of a cerebral thrombosis. Furthermore we have not had any such hematoma.

We have seen no cases of malignancy of the carotid body in our own patients or those of our associates over the years. The literature recounts quite a number and it is made clear in some of these presentations that such malignancies may make themselves manifest after a rather unusual time. The possibility of later malignant change in a benign carotid body tumor would certainly not be a compelling reason for operation. But it has been our experience that even small benign carotid body tumors are quite symptomatic. The large ones are even more so. Patients appear for treatment because they are troubled in the first place. There is always the matter of diagnosis. There are many other tumors which might have been carotid body tumors but which are operated upon and found to be more common lesions of the lymph glands, brachial cleft cysts, or rarer neurogenic tumors of other nerves or of the sympathetic chain. One of our extremely interesting tumors in the latter group was identified as a schwannoma. It arose from a very high level in the sympathetic chain on the left side and was actually removed through the space between the internal and the external artery. This left the patient with a Horner's syndrome.

It is our conviction that surgeons should feel no chagrin in abandoning the plan to remove the tumor when it is found that the situation cannot be coped with on the basis of hemorrhage, unfamiliarity with the entire situation, or if it seems that the circulation through the carotid vessels needs to be sacrificed. We have had experience of this sort in 1 case which unfortunately cannot be reported at this time because we do not have the entire record at our disposal. This patient was a soldier during World War II. His mass must have weighed 60 grams and

was explored by us on 2 occasions. First a biopsy was taken and we waited for permanent sections before proceeding with the second stage. The tumor was benign so at the second stage a very extensive approach and exploration was carried out. We were unable to remove it without sacrificing the carotid system. This was thought inadvisable. Postoperative x-ray irradiation was given. He was followed for some months. No improvement was noted. Unfortunately we do not have a late follow-up in this case. It is our observation that x-ray irradiation is not helpful in such instances. Ferrar, Kirkland, Judd and Devine¹ reporting the experience at the Mayo Clinic voiced the same concern regarding the necessity to preserve carotid vessels. There is no question that with the utilization of a meticulous and deliberate approach that experienced surgeons will find it possible to remove safely nearly all of these neoplasms.

CONCLUSIONS

Three classical cases of benign neoplasm of the carotid body were satisfactorily removed and are herein reported.

Reference is made to the general classification of organs allied to the carotid body. It is suggested that surgeons be on the alert for such tumors involving the carotid body bilaterally, the glomus jugulare, the nodules of the aortic arch and others which are similar to those of the carotid body.

It is advised that tumors suspected of being in the category of a carotid body tumor be explored surgically. When the tumor is found to be a carotid body tumor it is suggested that a meticulous and deliberate approach be made to remove it without disturbing the continuity of the common carotid and the internal carotid. It is thought advisable to abandon the operation without removing the tumor in the event that it is necessary to interrupt the continuity of the internal carotid artery. It is thought highly advisable to utilize one of the newer methods of restoring blood flow if it has already been disrupted.

Anticoagulant therapy beginning 2 hours postoperatively and continuing several days is recommended because of the possibility of late thrombosis.

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TECHNIC OF ARTERY VISUALIZATION

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The advent of direct surgical resection of arteries and their replacement has brought a demand for more accurate diagnosis. An exacting history and physical examination remain extremely important, and as experience is obtained they are relied upon more and more. In abdominal aortic aneurysms, the consistent possibility of resection being feasible below the renal vessels, has brought a marked decrease in the use of aortograms in these cases. Very little special equipment is necessary for the artery visualization technic described here (fig. 1).

The absence of femoral pulses in a patient with occlusive disease symptoms usually requires an aortogram for accurate diagnosis. The physical tests such as palpation or oscillometric tracing cannot be applied above the femoral level. It should be realized in aortic occlusion that the femoral pulses may be absent yet distal pulses be present. The presence of a good femoral pulse and absence of popliteal, posterior tibial and dorsalis pedis will usually require a femoral arteriogram for accurate diagnosis. This is done in an attempt to find an isolated segmental block which may be treated with a replacement graft. There must be an adequate outflow tract in any graft or failure is certain. Attempts to graft below the popliteal artery has always failed. The disease is always more extensive than the roentgenogram suggests. We have never been able to use as short a femoral artery graft as the roentgenogram seems to indicate.

We have oscillometric tracings, skin temperature tracings, and blanching and filling times performed on all our occlusive disease cases. Actually, the oscillometric tracings, pulse, and arteriogram measure the same effect. The skin temperature reading, blanching and filling with remote heat, measures in general, the sympathetic response and may influence the decision concerning sympathectomy. Previously we placed our patients on vasodilators and repeated these tests as an added indication for sympathectomy. However, we believe this as well as paravertebral sympathetic procaine block which was considered so necessary a few years ago, to be of no value due to the inconsistency of both procedures.

VISUALIZATION OF THE PULMONARY ARTERY

On occasions visualization of the pulmonary arterial tree is of importance. The diagnosis of an absent or hypoplastic pulmonary artery may be very satisfactorily diagnosed by the very rapid injection of 50 cc. of 50 per cent diatrizoate sodium through a #15 Robb needle and syringe in an antecubital vein⁵. This is a very simple procedure and we have not found it necessary to pass a catheter down the superior vena cava to obtain such pictures. We give our patients nembutal (100

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FIG. 1 Special equipment for arterial visualization. From left to right—30 cc. Bard aortogram syringe, 17 gauge aortogram needle, Parhad-Poppen 18 gauge needle, Robb angiocardigram needle, 50 cc. Robb angiocardigram syringe.

mg.) and morphine sulfate (10 mg.) one hour before the injection, and use 1 per cent procaine locally over the vein. The use of a multiple cassette technic is indicated so that the presence of an aberrant blood supply from the aorta may be visualized. Although rare, systemic blood supply to a portion of the lung may be cut during surgery, with resultant fatal hemorrhage. These vessels may be away from the hilum in what is considered a safe area. We use a Sanchez-Perez 11 by 14 inch 8 film cassette changer. Upon completion of the injection, with the needle attached directly on the syringe and taking approximately $1\frac{1}{2}$ seconds, four films are taken. The patient must hold his breath in inspiration during injection. This visualizes the pulmonary artery (fig. 2). After a delay which equals the difference between the arm-to-lung and arm-to-tongue circulation time, the other four films are taken for systemic arterial visualization. We believe that the direct connection of the needle to the syringe is important. Before this technic was used, the rubber tubes were blown off with resultant complete failure of the procedure. When the antecubital vein is very small, it is necessary to make a small incision over the vein and insert the needle directly. Usually when this is required, the vein is ligated; whereas, after percutaneous puncture this is not required.

THORACIC AORTA

Visualization of the proximal aorta is in general unsatisfactory. Excellent pictures can be obtained by passing a catheter down the external carotid artery.^{3, 4}



FIG. 2 Angiocardiographic visualization of right pulmonary artery and absence of left. The left lung was also bronchiectatic and pneumonectomy was performed.

This is a fairly complex procedure done in the operating room and following which the patient is transported to the Roentgenologic Department. Such a procedure invites infection. We have found the superior thyroid artery unsatisfactory as it is too small to accept the .066 inch inside diameter polyethylene tubing we believe necessary to obtain good visualization. The external carotid artery is isolated and a small opening made in the anterior wall while the vessel remains clamped using cord tapes. The measured amount of tube is then passed through this opening to near the aortic valve and 50 cc. of 50 per cent diatrizoate sodium (Winthrop Laboratories) is injected rapidly and 8 roentgenograms are taken using the rapid cassette changer set at $\frac{1}{2}$ second intervals. The left carotid is manually compressed during the injection and the right is occluded by the cord tapes (fig. 3). An identical procedure may be carried out using the femoral or brachial artery and passing the polyethylene tubing in a retrograde manner. This is a less extensive procedure in exposure, but the greater distance in passing the catheter retrograde against the pressure of the aortic blood flow makes it more difficult. We have had limited experience with the percutaneous retrograde methods of passing tubing from peripheral arteries.^{1, 2}

The procedure we prefer in proximal aorta visualization is the antecubital venous injection using the cassette changer. The arm-to-tongue circulation time is obtained and the exposure started 2 seconds less than this time with the timing being started at the beginning of the injection. The Robb needle and syringe



FIG. 3 Large thoracic aneurysm visualized by retrograde catheter technic from external carotid. This aneurysm was resected and replaced by homograft.

are again used. These films are not as dense as those made retrograde, but only occasionally will further study be required. In coarctation of the aorta, this procedure has been satisfactory in every way (fig. 4). The information desired is location and length of the coarctated region, and both are well shown by this technic. It is also useful as a diagnostic procedure when visualization of the aorta is desired in mediastinal masses (fig. 5). The differential diagnosis between tumor and aneurysm of the aortic arch is not uncommon, and this method is extremely simple in obtaining this information.

ABDOMINAL AORTA

There have been many technics for abdominal aorta visualization. Mechanical injections and multiple films as well as the use of two needles are advocated by some. We believe, however, that a single needle, single 14 by 17 film exposure, will give most of the information that can be obtained. We believe complex machinery should be avoided. The patient is positioned face down upon a 14 by 17 x-ray film with the lower border including both femoral arteries. We tried using 2 plates end to end under the patient and moving the x-ray tube 6 feet away. We abandoned this technic because the lower film was always by necessity poor quality and seldom added significant information. The left back is prepared and



FIG. 4 Angiocardiogram showing good visualization of coarctation of the aorta. This patient had coarctation resected at age 35, has had complete relief of his symptomatic hypertension and lower extremity claudication.



FIG. 5 Angiocardiogram showing the anterior mediastinal mass to be separate from the aorta. A small second intercostal incision was made and diagnosis of metastatic carcinoma made.



FIG. 6 Anteriogram showing terminal aorta and left common iliac narrowing. Note the tip of needle is at T-11 level. Resection and homograft replacement was done with much more extensive disease found than indicated here.

draped and intravenous sodium thiopental anesthesia is begun. A #17 aortogram needle is inserted at a 45 degree angle upward and 45 degrees medially, the skin entrance being four fingerbreadths left of the midline at the level of the twelfth thoracic vertebra. The body of the vertebrae is thus encountered after which the needle is withdrawn slightly and passed just anterior to the vertebrae. The stylet is removed and the jet of blood is obtained. A curved clamp with the curve downward is then placed on the needle at the skin level to prevent pushing the needle through the aorta, and a large bore short barrel 30 cc. syringe containing 35 cc. of 50 per cent diatrizoate sodium which is placed in the syringe just before injection is connected directly to the needle. This dye is injected as rapidly as possible with the film being taken upon command when about 5 cc. of dye remains in the syringe. We believe the use of diatrizoate sodium is preferable (fig. 6, 7, 8).

We have abandoned the use of aortograms in aneurysms (fig. 9). We believe it is not worth the risk involved in the procedure. We, however, continue to use it in arteriosclerosis and it is of some importance in the evaluation of resection. We do not use aortograms routinely after aortic resection; but have in instances where patients have recurrent difficulty. A rather high percentage of our patients postoperatively complain of burning in their feet and toes after exertion and aortograms in these patients have shown no evidence of insufficient filling. If an intravenous pyelogram has not been previously made, we keep the patient in x-ray and complete such a study.



FIG. 7 This aortogram shows a complete external femoral artery block which was treated by endoarterectomy with excellent results.



FIG. 8 This aortogram shows occlusion at the renals. At surgery, both renals were partly occluded by plaque from the aorta. This was removed and homograft of aorta below was performed. He is still hypertensive and has no function of left kidney.



FIG. 9 Flat plate of abdomen showing outline of calcified aneurysm. The resected aneurysm is projected after homograft replacement.

FEMORAL ARTERY

Surgery of arteriosclerosis obliterans remains today as in the past, predominately amputation. However, with the use of grafting procedure, we may on some occasions return a patient to a relatively normal status (fig. 10). The selective use of lumbar sympathectomy gives very excellent palliative results on occasions (fig. 11). Unless the patient has constant pain we expect 50 per cent to improve following sympathectomy. Sympathectomy, of course, gives excellent results in healing of skin lesions from arterial deficiency and we have never seen a gangrene made worse by sympathectomy. If a patient has a palpable femoral pulse of fair to good quality and no distal pulses, we consider him a candidate for femoral arteriogram. Oscillometric tracings are also used although the arteriogram more accurately determines the outflow tract.

We use general anesthesia in this procedure. The total anesthesia time is seldom over 2 minutes. Arterial spasm is minimized and the procedure is more comfortable for the patient. The inguinal region is prepared and draped and the anesthesia is started. A #18 Poppen needle is used with the left hand stabilizing the artery at the level of the inguinal ligament. The needle is inserted caudally with a 5 cc. syringe filled with normal saline solution attached. When arterial blood flows into the syringe, a syringe with 20 cc. of 30 per cent diatrizoate sodium is connected. Ten cc. of the dye is injected over a 5 to 7 second interval to allow the dye to pass through collaterals to the distal main branch. The re-



FIG. 10 A short segmental block of femoral artery which was treated by homograft bypass graft with excellent result.



FIG. 11 Femoral occlusion considered not a candidate for graft due to small size of distal vessel. Good relief of claudication from sympathectomy.



FIG. 12 Segmental block treated by homograft which thrombosed. Notice the marked disease in the distal vessel.

maining 10 cc. is then rapidly injected and a single 14 by 17 film is taken at completion of the injection (fig. 12). The oscillometric tracing and palpation of the pulse in the thigh give a good indication as to the level of the block and the film can be adjusted according to these findings (fig. 13). We allow the patient to awaken as soon as the injection is completed, as we never give more than one injection of dye in one day.

We have used arteriograms only occasionally in arterial emboli (fig. 14). We believe that the sudden onset of pain in the leg and the location of the coldness and discoloration a few inches distant to an arterial bifurcation makes the diagnosis and location without further inquiry. Emboli usually lodge at bifurcations as the branches are naturally smaller than the parent artery. In arterio-sclerotic vessels the caliber may be smaller in a bizarre location. In this type of case, an arteriogram will be useful.

PITFALLS AND COMPLICATIONS

The outstanding pitfall in the use of aortograms and arteriograms is the poor correlation between the findings on x-ray and at surgery. Arteriosclerosis is a generalized disease and it is a rare case indeed in which there are areas of completely normal artery. X-ray films are two dimensional pictures, and a plaque in the proper plane may cause a 50 per cent occlusion and still show as a normal width on arteriography (fig. 15). It is seldom that the vessel is less diseased than is seen on arteriogram (16, 17, 18, 19).



FIG. 13 Multiple aneurysms in femoral artery graft, replaced again by homograft which thrombosed. This patient has a nonspecific arteritis.

The problem of direct irritation by the needle and dye is poorly understood. It is a well observed fact that there is a great variation in peripheral pulses in patients with arteriosclerotic disease. Examination therefore must be performed more than once before decisions concerning arteriograms can be made, as a



FIG. 14 Arteriogram showing occlusion at midhigh due to an embolus. Embolectomy performed and the vessel found markedly arteriosclerotic at this level explaining the lodgement.

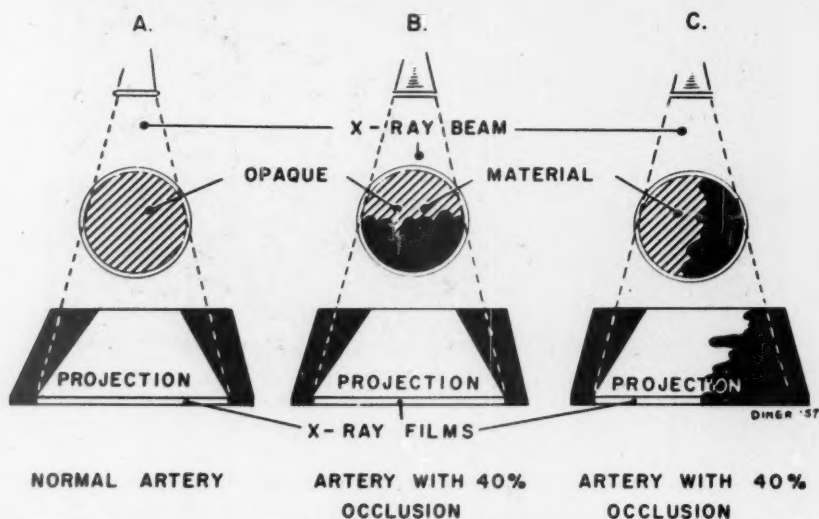


FIG. 15 If a plaque should be in the proper plane a marked occlusion may occur without appearing narrow on x-ray film. The difference in density will not be apparent.



FIG. 16 Aortogram showing complete block of left iliac and apparent normal right iliac. As can be seen in the projected specimen, the right iliac was also markedly narrowed.

pulse may not be found one day and actually be of fair quality the next. We believe this unknown factor may make general anesthesia preferable.

The problem of injection of the wrong artery in the abdomen should seldom be a problem. If the aortogram needle is passed correctly, there must be a vas-



FIG. 17 If the aortogram alone had been considered an isolated left iliac block would have been suspected. Clinically bilateral partial occlusion was suspected and found at surgery.

cular abnormality to inject the renal, superior mesenteric or celiac artery. These vessels arise at about L-2 and if directed correctly, the aortogram needle should be no lower than T-12. However, when there is a high aortic block, the renal artery may receive a high pressure of highly concentrated dye and a fatal renal shutdown may result. For this reason, we strongly object to mechanical injectors—the feel of the resistance encountered will prevent this complication in a large percentage of the cases.

Extravasation of dye in aortograms has occurred only twice in our experience. In one case where 70 per cent sodium acetrizoate was used, a rather severe reaction resulted requiring narcotics for 3 days. However, in another case where hyopaque was used, only slight discomfort resulted. We believe using a clamp at skin level to keep the aortogram needle exactly in the aorta is important. We have had no extravasations in femoral artery injections. We attribute this to the Parhad-Poppen needle, which is inserted for some distance into the femoral artery.



FIG. 18 In this case both iliacs filled but at surgery only a very small lumen remained. On the left side the graft extended to the femoral artery.



FIG. 19 This arteriogram shows a badly diseased femoral artery, but the segment of popliteal visualized appears relatively small. At surgery there was marked intimal proliferation.

In severe disease in which the blood supply to the feet is precarious, there is some danger in further damage from dye injection due to arterial spasm. Such spasm is less marked in the extremity with a poor blood supply as the smaller vessels are less rapidly injected. We have observed a correlation between the temperature of the foot immediately after injection and the degree of occlusion in femoral arteriograms. The normal extremity will become quite cool for several minutes; whereas in a markedly narrowed vessel the temperature remains relatively unchanged.

Drug reactions are an ever present problem. There is very poor correlation between the skin and conjunctiva testing and sensitivity. The general impression is that a peripheral intraarterial injection is less likely to give a fatal reaction than intravenous injection. The relative safety of hyopaque, we think, makes it the drug of choice.

Difficulty in injection may occasionally be encountered if the dye is drawn into the syringe too soon, as the plunger may stick to the syringe. This will slow the injection to such a degree that the contrast is poor.

SUMMARY

The technic currently used for visualization of arteries are presented. We have changed these technics from time to time and claim no originality for any of them. Illustrations are presented to show what may be expected using these technics.

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AN HISTORIC APPROACH TO ANTIBIOTIC RESISTANCE

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The phenomenon of bacterial resistance to specific antibiotics has become of increasing importance in clinical medicine. The sulfonamides and penicillin were very effective in the treatment of war injuries in World War II. After these and other potent antimicrobial agents became available, infections which previously had been difficult to control were frequently easily eradicated. An example of this was the marked success that occurred in the treatment of fulminating streptococcal infections with penicillin. It was probably during this period, when "clean" surgical wound infections were relatively rare, that a certain contempt for the ubiquitous staphylococcus and perhaps even for rigid aseptic technic developed. By "clean" surgical wound infections is meant the infection of those wounds which are made in the operating room under standard, aseptic technic, and in which healing *per primum*, without suppuration, would ordinarily be expected. This is in contrast to accidental and battle injuries, or surgery on already infected areas. A renewed interest in surgical wound infections developed beginning in the late nineteen hundred and forties. This coincided with an increasing incidence of "clean" surgical wound infections, frequently occurring in the form of small "epidemics".

Besides the obvious occurrence of antibiotic-resistant bacteria in wound infections, the surgeon may meet these organisms in such varying locations as the lung in super-infected postoperative pneumonitis, the skin in burns, and the gastrointestinal tract in pseudomembranous ileocolitis following broad spectrum antibiotic therapy. To help lend some perspective to this problem the early history of the antibiotics and the history of antibiotic resistance is presented.

EARLY HISTORY OF THE ANTIBIOTICS

Sir H. W. Florey¹⁶, in his historic account of the introduction of penicillin and other antibiotics reviewed the history of microbial antagonism. The folklore he quoted, suggesting the use of a fungus in medicine, included observations from Mexico, Brazil, the Ukraine, Central Europe, Yugoslavia, and England. Observations on bacterial antagonism were made prior to the work of Pasteur and Joubert (1877), but they were credited with the first scientific demonstration of this phenomenon.

The use of pyocyanase from *Pseudomonas pyocyanea* (*Pseudomonas aeruginosa*) is the first example of the treatment of human disease by the injection of bacterial products from an organism other than the one that caused the disease. Pyocyanase was introduced into medicine in 1899 by Emmerich and Löw. Boris Sokoloff¹⁸ told of the enthusiasm of Metchnikoff, a close collaborator and

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friend of Pasteur, in talking of the constant struggle for existence between microorganisms. Metchnikoff was excited over the discovery of pyocyanase, and suggested that research on it be conducted in the Pasteur Institute.

It had often been assumed that a differential antibacterial action was unknown among antibiotics before the description of the action of penicillin¹⁵. This was, of course, not the case, for it had several times been brought out in the pyocyanase work.

Florey¹⁶ gave some perspective to the discovery of penicillin and related it to the work on pyocyanase:

"When the reader has further considered the chemical, bacteriological, and animal experiments which have been carried out with *Ps. pyocyanea*, he will appreciate that the work done with this organism was comparable in scope and in imagination with the outburst of energy in the antibiotic field which began in 1940. There can be little doubt that much of the work was incompetent, just as much work today is incompetent, but some of it showed efforts at bacteriological control of clinical results, and it is difficult to believe from the records that pyocyanase was worthless when properly prepared in an active state, as it appears to have been around 1908. These older workers had nearly all the ideas which are too readily supposed to be of quite recent origin—their misfortune was that they happened to be working with a rather toxic antibiotic preparation."

Proteolytic bacteria were utilized for a while in the treatment of wounds. Spore forming bacteria such as *B. subtilis* have been known to produce antibiotic substances. The plant and soil microbiologists were aware of the constant struggle between the microorganisms in nature long before the clinical microbiologists. The antagonistic effect of the actinomycetes, yeast, and fungi on bacteria had been known since the late nineteenth century.

Sir Alexander Fleming's¹⁵ own description of his discovery of penicillin is certainly worth quoting:

"The contamination in 1928 of a culture plate by spores of a species of *Penicillium* was the beginning of the study of penicillin. Such contamination is not uncommon in a bacteriological laboratory and is usually regarded as a reflection on the technique of a bacteriologist. Sometimes, however, it is unavoidable, as in this particular instance when the culture plate had to be opened for examination under a dissecting microscope and then left for future examination. When next observed, mould spores which had gained access had developed into a large colony. This in itself did not call for comment, but what was very surprising was that the staphylococcal colonies in the neighbourhood of the mould, which had been well developed, were observed now to be showing signs of dissolution. This was an extraordinary and unexpected appearance and seemed to demand investigation."

It had been observed during World War I that the antiseptics used were at least as toxic to the tissues as they were to the bacteria. Lister, himself, had made similar observations and had searched for substances less toxic than the carbolic acid he had originally introduced. Fleming recognized that the leukocytes should remain viable and that the commonly used antiseptics destroyed them in the concentrations needed to kill the bacteria. The penicillin containing broth filtrate of Fleming was more toxic to bacteria than to leukocytes and other animal cells. In this respect it differed from the other known antiseptics of that day.

After this original work little was done with penicillin for a number of years.

Then the discovery of prontosil in 1935 by Gerhard Domagk, Director of the Institute of Experimental Pathology of the I. G. Farbenindustrie in Germany, and the introduction of several sulfonamides gave impetus to the study of systemic chemotherapeutic agents.

H. W. Florey, and associates¹⁶ commented that penicillin probably would not have been developed in the face of all the difficulties of production had it not been discovered at Oxford that it was a systemic chemotherapeutic agent. The Oxford group, of course, was instrumental not only in initiating the first clinical trials of penicillin, but also in expediting its mass production in the United States.

With the beginning of the large-scale production of penicillin, an intense search for better strains was made. The original strain of Fleming remained about as good as any, however, for surface cultures. In 1943 a strain of *Penicillium chrysogenum* from a mouldy patch on a cantaloupe was found in Peoria, Illinois, which increased the yield of penicillin, using the submerged culture method developed there at the Northern Regional Research Laboratory of the Department of Agriculture.

Selman A. Waksman had done much of his early research with the soil microorganisms. After the discovery of streptothricin and the rapid development of penicillin, it was obvious to him that there was need for an antibiotic effective against gram-negative bacteria and the tubercle bacillus. In September 1943, he and his assistants isolated an antibiotic which possessed properties similar to those of streptothricin, but was less toxic. This antibiotic was called streptomycin, having been isolated from the actinomycete *Streptomyces griseus*. Waksman's⁵³ description of the antagonistic relations of microorganisms, written in 1941, can hardly be improved upon today, even after the discovery of countless newer antibiotics:

"Ranging between the phenomena of true parasitism, where one organism lives in or upon the living body of another, and true saprophytism, where one organism merely destroys the waste products and dead cells of the other, there is a group of relationships between living systems which may be designated as associative and antagonistic; in the first, one organism assists the other, whereas in the second, one organism is injurious to the other. There is increasing appreciation of the fact that nature harbors many unknown organisms that are capable of combating disease-producing bacteria, fungi, worms, and insects. Our knowledge of the activities, potentialities, and importance of these microbes is still incomplete. Man, in his struggle for existence, succeeded, before the development of microbiology, in domesticating and utilizing the activities of many microbes. However, these represent only a small fraction of the microbial world. It is possible that we are finally approaching a new field of domestication of micro-organisms for combating the microbial enemies of man and of his domesticated plants and animals."

The history of the discovery and introduction of countless antibiotics after penicillin and streptomycin illustrates their biologic and economic importance.

HISTORY OF ANTIBIOTIC RESISTANCE

The introduction of the sulfonamides and the antibiotics has had a tremendous influence on the treatment of wound infections. Infections caused by bacteria that were resistant to the antibiotics generated marked interest in many fields.

The concept of antibiotic-resistant microorganisms is of course a recent one, although there are examples of cultures of certain resistant bacteria that were obtained prior to the introduction into therapy of the specific antibiotic to which they are resistant. Strains of the *Micrococcus pyogenes*, var. *aureus*, the current name for the *Staphylococcus aureus*, which were naturally resistant to penicillin were isolated before penicillin was used on human beings. Reports by Kirby³⁰ in 1944 and by Bondi⁷ in 1945 documented this phenomenon.

In 1942 Rammelkamp and Maxon⁴⁵ found an increase in the resistance of strains of staphylococci isolated from the patients during the course of treatment of localized infections.

In 1947 Barber¹ reported an increase in the percentage of strains of penicillin-resistant *S. aureus* recovered from infected lesions at the Hammersmith Hospital of the British Postgraduate Medical School. This increase was from 14.1 per cent in 1946 to 38 per cent in 1947. She also pointed out that there was a higher incidence of penicillin-resistant *S. aureus* of the same phage reaction isolated from one ward of the hospital. In subsequent articles Barber and associates^{2,3} reported a further increase in penicillin-resistant strains of staphylococci and focused attention on the import of the nasal carrier state for this organism.

Reports of this problem have come from many areas of the world. In Australia, Rountree and Thomson⁴⁷ wrote of their studies in the Royal Prince Alfred Hospital of Sydney. They found that 54.5 per cent of 200 members of the hospital staff were carriers of staphylococci; 80 per cent of these were penicillin-resistant strains. A common pattern was resistance to penicillin, streptomycin, chlortetracycline, and oxytetracycline. Many of the strains isolated were of the same phage type. These authors⁴⁶ had previously reported on the resistance of *S. aureus* to penicillin and streptomycin and also on the importance of the nasal carriers.

From Bergen, Norway, Vogelsang and Boe⁵¹ reported that 18 per cent of patients had resistant *S. aureus* on admission to the hospital, and 42 per cent when discharged. Vogelsang⁵² reported further studies on the hospital staff. From 746 members of the staffs of 3 hospitals in Bergen he recovered 452 pathogenic strains of *S. aureus* from the throats, and 437 strains from the noses. In the studies at the University of Chicago a much higher ratio of nasal carriers to throat carriers for staphylococci was found. Vogelsang further found that the staff of the Medicine Department of the larger of these 3 hospitals had a 58 per cent carrier rate, while the staff of the Surgery Department had a 55 per cent carrier rate of resistant staphylococci. The staff with no patient contacts harbored 18 per cent resistant strains, which was comparable to that of patients on admission to the hospital and to that of medical students returning after a 2 month vacation. This finding corresponds with the subsequent observation that the carrier rate is related, in general, to the exposure rate. At the University of Chicago Clinics the surgeons had a higher rate of Staphylococci and other potential pathogens than did the ancillary surgical personnel.³³

Gould and McKillip¹⁷ in Edinburgh found 7 times more penicillin-resistant strains in people receiving this antibiotic. Berker and Napp⁵ in Hamburg found

an increase in resistant staphylococci among patients after 4 days in the hospital, and also a higher percentage among patients in the Gynecology and Surgery Clinic, than in the Psychiatry Clinic. Hedlund²² reported that the resistant *S. aureus* had become an increasing problem in the Contagious Hospital of Stockholm, and Wallmark²⁴, from the same city, noted that a large percentage of superficial purulent lesions in outpatients was due to antibiotic-resistant *S. aureus* of several phage types.

Many reports of the increasing occurrence of antibiotic-resistant staphylococci have been made in this country. Studies by Needham and Nichols⁴¹, ⁴² Spink⁴⁹, Kirby and Ahern³¹, Benham, Havens, and Landy⁴, ²¹, ³², ³³ and many others illustrated this. Finland and Haight¹⁴ isolated 500 strains of hemolytic, coagulase-positive *S. aureus* from clinical material at the Boston City Hospital from October 1951 to February 1952. About three-fourths of these strains were resistant to penicillin, one-fourth to chlortetracycline, and one-third to oxy-tetracycline.

Many of the above reports substantiated the finding that the over-all incidence of penicillin-resistant staphylococci is related to the amount of this antibiotic used within the community. A study carried out by the Army Medical Service Graduate School²⁴ further supported this. Staphylococci isolated from cutaneous lesions in tropical Mexico were all sensitive to low concentrations of penicillin. Another example of theirs seems most pertinent: staphylococci isolated from North Borneo were all sensitive to penicillin in very low concentrations, whereas those isolated from Kuala Lumpur, which is just across the straits, needed a higher range of concentrations of penicillin to be effective. The economic standard is much higher in this area than in North Borneo and the amount of penicillin used is far greater, correlating with the increased resistance.

The mode of transmission of staphylococci has engendered considerable interest in recent years. It can be noted that Girolamo Fracastoro (Fracastorius, 1478?-1553) in his treatise *On Contagion, Contagious Diseases and Their Cure* gave us a very modern view on the role of fomites in the possible spread of disease¹⁰.

"It is indeed wonderful how the infection of phthisis or pestilential fevers may cling to bedding, clothes, wooden articles, and objects of that kind for two or three years, as we have ourselves observed."

Eric Stone⁵⁰ pointed out that the American Indians were known to keep their wounds clean, and in their clashes with the white man their wound treatment often gave better results than that of their enemies. The white soldiers were exposed to hospital gangrene while the Indians were treated in isolated lodges.

Duguid and Wallace¹³ found that a large number of bacteria-carrying dust particles were liberated from the skin and clothing by even the slightest activity; very vigorous activity liberated many times this number of particles. About 10 per cent of these particles remained air-borne for a half hour. *S. aureus* was present in about 0.1 per cent of the bacteria-carrying dust particles which entered the air from the clothing of carriers. Clarke, Dalgleish, and Gillespie⁸ were able

to recover resistant staphylococci from ward air and dust as well as the noses of the patients and the hospital staff. Furthermore, the number of organisms recovered was roughly related to the amount of antibiotics used in these wards, leading to their opinion that cross infections appeared to be a very important source of these infections. These same authors, together with Parry⁹, reported on the decrease in dust particles by oiling the floor and bed clothes in a surgical ward; however, this did not decrease the nasal and wound cross infection rates. Blowers, and associates⁶ reported in 1955 their extensive studies on the potential sources of spread of resistant staphylococci. These studies were carried out in a new thoracic hospital, built in 1952, in which post-thoracotomy wound infections caused by antibiotic-resistant strains of *S. aureus* became a serious threat. A partial list of the sources from which they were able to recover large amounts of staphylococcal dust included the following: corridor floors, blankets after laundering, dust of underclothing even when covered with sterile gowns, movement of the patient from the cart to the operating table, spray in pump aspirators, operating room lamps, gauze masks, punctured gloves, unnecessary movements in the operating room, excessive opening of operating room doors, talking during surgery, and improperly functioning air ducts. After this preliminary study extremely detailed and rigid measures were instituted to correct these defects. Blowers and associates⁶ reported that the rate of "clean" surgical wound infections then decreased to about one-half, except when an outbreak occurred, which was later traced to a nasal carrier of an antibiotic-resistant *S. aureus*. This latter is significant, for it appears that a single unsuspected upper respiratory carrier of antibiotic-resistant *S. aureus* can negate the most meticulous attempt to reduce the staphylococcal contaminations from all other sources.

Hare and Thomas¹⁹ found the anterior nares the most important location of resistant staphylococci, and that the throat was relatively unimportant as a source of this organism. They also noted that expulsion, except when snorting, was a rare cause for the dissemination of these bacteria. Furthermore, they thought that the swallowing of these organisms and expulsion through the feces was also not an important source of their dissemination. Dowling, Lepper, and Jackson¹² reported on the higher incidence of antibiotic-resistant strains of *S. aureus* in patients who were hospitalized, and their spread to family contacts after these patients were discharged.

The role of resistant staphylococci in "clean" surgical wound infections is of considerable clinical importance. Reports of Miles³⁸ in which he discussed the mode of spread, and of Miles, Williams, and Clayton-Cooper³⁹ in which they described the importance of the carriage of *S. aureus* are among some of the earlier reports. Harrison and Cruickshank²⁰ noted that from 10 to 15 per cent of surgical cases with thorocoplasty had staphylococcal wound infections. Howe²⁶ noted a stepwise increase in major wound infections at the Massachusetts Memorial Hospital from 1.09 per cent in 1949, 1.77 per cent in 1950, 1.98 per cent in 1951, 2.51 per cent in 1952, to 3.98 per cent in 1953. Howe reported at the Forum on Fundamental Surgical Problems of the American College of Surgeons²⁷ in October 1956, and also in the New England Journal of Medicine²⁸ that by instituting a

program to prevent cross contamination with *S. aureus* the wound infection rate has decreased at the Massachusetts Memorial Hospital. A few of the many reports on the treatment of surgical wound infections were by Pulaski^{43, 44}, Weinberg⁵⁵, Howe²⁸, and Meleney^{36, 37}.

An interesting study by Lepper and associates²⁵ showed an increase in erythromycin-resistant staphylococci from 0 to 75 per cent among hospital workers during a 5-month period when this drug was being used more frequently than any other therapy in the involved hospital. This rate decreased from 75 per cent to 35 per cent after erythromycin was withdrawn. The most important observation was that there was a concurrent increase in the carrier rate of tracheotomized patients of erythromycin-resistant staphylococci from 0 to 95 per cent. Many other reports of the occurrence of erythromycin-resistant *S. aureus* followed the laboratory and clinical studies on erythromycin by Haight and Finland¹⁸. One such report from London by Hobson²³ showed that resistance to erythromycin developed stepwise as with penicillin. He found that the erythromycin-resistant staphylococci differed from the erythromycin-sensitive organisms only by a slight difference in growth rate and an acquisition of cross resistance to carbomycin.

Antibiotic-resistant staphylococci are important in many phases of medicine other than in surgical wound infections. In pediatrics such conditions as gastroenteritis³⁴ and acute mastitis of the newborn⁴⁰ have been traced to antibiotic-resistant micrococci. Johnson and Hurst²⁹ described a patient with bacterial endocarditis due to a penicillin-resistant staphylococcus; he was then treated with intravenous oxytetracycline and erythromycin, as well as intramuscular streptomycin, to control the infection. Dearing and Heilman¹¹ were among the first to describe pseudomembranous ileocolitis following broad spectrum antibiotic therapy. This was associated with an overgrowth of antibiotic-resistant *S. aureus* in almost pure culture. A number of deaths have occurred from the fulminating diarrhea that accompanies this disease.

Another clinical entity related to antibiotic therapy is that of superinfection. Weinstein, Goldfield, and Chang⁵⁶ found 3.19 per cent superinfections in a series of more than 3,000 patients. This usually occurred on the fourth or fifth day after the beginning of antibiotic therapy and most frequently involved the same organism in the primary and secondary infection.

Perhaps the most recent aspect of this whole problem that the physician should be aware of is the increase in the number of "clean" surgical wounds and other infections caused by enteric bacteria i.e. *E. coli* and strains of *Pseudomonas* and *Proteus*. These organisms exhibit a wide range of different sensitivity patterns. This has been related to the upper respiratory carrier rate³³.

SUMMARY

The early history of the antibiotics has been described, followed by a review of a number of aspects of antibiotic resistance. It is well known that antibiotic-resistant strains of *Staphylococcus aureus* have been isolated from all over the world, and it is perhaps equally well known that a number of these strains have

been a very important source of surgical wound infections as well as other types of infections. Perhaps two other aspects of this broad problem should be emphasized here: (1) the importance of the nasal carrier of antibiotic-resistant bacteria, and (2) the increasing number of infections containing enteric bacteria. Awareness of this over-all situation may possibly be as helpful to the physician in the long run as specific suggestions for diagnosis and treatment. This awareness, together with a reemphasis of classical concepts of sterile technic and the full utilization of modern laboratory controls of infection, will allow the physician to intelligently deal with this changing problem of antibiotic-resistant bacteria.

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SOME CLINICAL OBSERVATIONS ON THE USE OF 21-HYDROXY-
PREGNANEDIONE SODIUM SUCCINATE (VIADRIL®)*
IN GENERAL ANESTHESIA

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The use of steroids to produce general anesthesia is a new concept that has developed within the past year or so. Seyle,⁸ while investigating several steroids in 1941, noted that certain ones produced varying degrees of basal narcosis or anesthesia in certain species of animals. The recent literature^{1, 5, 6, 7, 8} reveals several reports of the use of 21-hydroxypregnanedione sodium succinate (Viadril) for the production of anesthesia in both animals and man. Several of these reports^{1, 3} indicate a rather high incidence of thrombophlebitis as the chief deterrent to accepted usage of Viadril. It was decided to evaluate this drug by use of dilute solutions and observe its anesthetic properties, and to determine if possible the advantages or disadvantages of various strength solutions.

METHODS

Viadril solutions of 0.5, 0.75 and 1.0 per cent were prepared using either 5 per cent dextrose in water or normal saline solution as the diluent.

The solution was permitted to drip at a very rapid rate through a three-way stopcock and an 18 gauge needle, which had previously been placed in a large vein. We carefully ascertained the proper placement of the needle. If there was complaint of pain, the drip of Viadril solution was stopped and a rapid infusion of 5 per cent dextrose solution was started simply by changing the direction of the stopcock. As soon as the pain had diminished the solution of Viadril was again permitted to run at a rapid rate.

In order to arrive at a more or less constant endpoint to determine depth of narcosis, disappearance of the wink reflex was chosen as the arbitrary time at which sleep occurred. In the first patients the drug administration was discontinued at this point, however in order to obtain a greater depth of "anesthesia" precalculated doses were administered and the disappearance of the wink reflex recorded only to obtain induction time.

All patients were premedicated in the usual manner prior to their coming to surgery. No attempt was made to select patients from the standpoint of age, physical condition, or type of procedure contemplated. One standing rule however prevailed, that of a well-placed, large bore needle in a vein that was not obviously diseased.

In this series of patients Viadril was administered to 114 individuals ranging in ages from 1½ to 92 years. The drug was used in two general ways. Viadril

Supplies of Viadril® were made available by The Chas. Pfizer & Co., Inc. of Brooklyn, N. Y.

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TABLE 1
Showing case distribution

Strength of Solution	Induction Agent for General Anesthesia	Supplement to Regional Anesthesia	Total
0.5%	35	19	54
0.75%	25	7	32
1%	25	3	28

TABLE 2
Average dosage and sleep time

Strength of Solution	Average Dose	Average Time for Disappearance of Wink Reflex	Rate of Flow
0.5%	909 Mg.	8.7 minutes	Rapidly as solution would flow
0.75%	1209 Mg.	6.8 minutes	Do
1.0%	1405 Mg.	5.6 minutes	Do

was used 85 times as an induction agent followed with either gaseous or volatile agents, or a combination of these two. It was used 29 times as a supplement to regional anesthesia, or administered in small repeated dosage to patients under regional anesthesia in order to determine length of action (table 1).

RESULTS

After 4 or 5 minutes of administration of Viadril all patients, with the exception of one, went quietly to sleep without excitement or disturbance. The one exception was an 18 month old child who after receiving 125 mg. became very spastic, then cyanotic and frankly convulsed. Upon the administration of oxygen the seizure terminated within a minute or so. The time of disappearance of wink reflex varied with different individuals, the more robust taking a longer period of time, the more debilitated much less time. The average times are best demonstrated in table 2.

The rate of administration was approximately the same for the various strength solutions, therefore the 1.0 per cent solution was expected to produce sleep more rapidly than did 0.5 per cent solution, and that is exactly what took place.

Some elderly patients, under regional anesthesia, who were complaining of pain or discomfort for various reasons, went quietly to sleep on relatively small doses of the drug. They did not exhibit the confusion or disorientation that we commonly see following the administration of the thiobarbiturates. In about 30 minutes these patients would awaken, respond to questions, then go back to sleep with an additional dose of Viadril. In these instances subsequent intermittent dosages were almost equivalent to the original dose necessary to produce sleep.

Contrary to many reports,^{1, 3, 4, 5, 6, 7} we did not find adequate pharyngeal or laryngeal relaxation for endotracheal intubation. Of the 85 patients in whom Viadril was used as an induction agent for general anesthesia, 54 patients were intubated. In only 5 patients was it possible to visualize the larynx and insert an endotracheal catheter without the use of a muscle relaxant or by increasing the depth of anesthesia with another agent. Possibly sufficient time was not allowed to elapse or sufficient dosage had not been administered prior to attempting the endoscopy. The five exceptions were all below average in weight and in general physical condition, and each had received 1500 mg. of the drug. These 5 patients we thought to be relatively over-dosed.

Most instances in which general anesthesia was induced by Viadril, less concentration of inhalation agents was needed initially to provide adequate depth of anesthesia. Within 30 or 40 minutes many of these patients were in too light a plane for adequate surgical manipulation. Only in the aged patients, in whom too much drug had been given initially, was nitrous oxide supplement sufficient for continuation of the procedure. Muscle relaxation was variable and it was usually necessary to deepen the level of anesthesia or use a muscle relaxant for adequate relaxation.

In 2 patients hiccup developed shortly after induction with Viadril. This persisted for 5 minutes in one instance and 10 minutes in the other, both ceased spontaneously. Laryngospasm was not observed in any patient receiving Viadril.

Changes in respiratory pattern became apparent in most instances as soon as anesthesia was produced. This usually was typified by an increase in rate and a decrease in tidal exchange. This was not significant when 0.5 per cent solution was used, as adequate ventilation was maintained without assistance. As concentration of solution and dosage was increased, respiratory depression became more profound. It was necessary to assist respirations in about 90 per cent of the patients who received the 1.0 per cent Viadril solution to maintain adequate ventilation. One patient in this group developed apnea which persisted for 20 minutes.

The most striking changes however occurred in the systemic blood pressure. In the group receiving 0.5 per cent solution of Viadril little significant change took place. In the group receiving 0.75 per cent solution there was an average decline in blood pressure of 15 mm. of mercury. In the 1.0 per cent group the drop was both significant and many times alarming; the average fall was 53 mm. of mercury. In this latter group the greatest changes were noted in the hypertensive patients, some of which sustained blood pressure drops of as much as 110 mm. of mercury.

Many of the minor blood pressure changes were self-limiting lasting only a few minutes with return to near normal levels within 10 or 15 minutes. If the change was evaluated as one of consequence, a small dosage of a vasopressor promptly produced a return to normal levels. In 2 patients who sustained alarming drops in systemic blood pressure, neither methoxamine or mephentermine produced any response, however with intravenous administration of 25 mg. of ephedrine the blood pressure promptly returned to its previous level and remained there.

TABLE 3

Alterations in respiration and circulation with various strengths of Viadril

Strength of Solution	Respirations	Apnea	Blood Pressure	Pulse Rate	Arrhythmias
0.5%	Little or no depression	None	Very little change	Little change	None
0.75%	Pronounced depression in 80%	None	Average decrease 15 mm/Hg	Little change	None
1.0%	Profound depression in 90% of cases	1 Case	Average decrease 53 mm/Hg.	Little change	Three—all supra-ventricular

TABLE 4

The incidence of pain and thrombophlebitis

Strength of Solution	No. Cases	Pain on Injection	Thrombophlebitis		% Thrombophlebitis
			Mild	Severe	
0.5%	54	4	1	0	1.8
0.75%	32	4	2	1	9.4
1.0%	28	11	3	1	14.2
Total.....	114	19	6	2	7% Av.

In trying to reproduce this same phenomenon in dogs it was found that in normotensive animals the degree and rate of fall of the systemic blood pressure was correlated directly with dosage and rate of administration. Also it was demonstrated that in the grossly overdosed animal, not only did the blood pressure fall, but the hypotension persisted unless corrected by a vasopressor. One vasopressor seems to be as efficacious as the other, methoxamine or ephedrine.

It was further demonstrated that in the animal whose respiration was markedly depressed with Viadril or who was rendered apneic, blood pressure was more profoundly depressed. If respirations remained nearly normal and adequate, blood pressure changes were transient and self-limiting.

It would seem that most of the circulatory changes are evident when large doses in concentrations above 0.5 per cent are used and when single dosage is increased above 1000 mg.

Arrhythmias (table 3) were seen only when 1.0 per cent solution was being used. In all 3 instances single 1500 mg. doses of 1.0 per cent solution were administered. These were sinus arrhythmias, transient in character, disappearing spontaneously in from 20 to 30 minutes.

THROMBOPHLEBITIS

Table 4 shows the progressive increase in the incidence of thrombophlebitis as the percentage strength of solution increases. Postoperatively the recipient vein was examined daily; leading questions were avoided. Tenderness over the vein that cleared in 2 or 3 days was classified as mild thrombophlebitis. More

involvement was classified as severe. There were only 2 in this category and both had begun to resolve within 7 or 8 days. The one mild thrombophlebitis that developed in the 0.5 per cent group was in a small vein on the dorsum of the hand.

Dent and Stephens³ report an over-all rate of thrombophlebitis of 77 per cent with 2.5 per cent solution of Viadril. Burstein² reports no cases of thrombophlebitis where 0.1 to 0.4 per cent solution was used in 500 patients. Table 4 shows 1.8 per cent thrombophlebitis in 54 patients where 0.5 per cent solution was used, 9.4 per cent in 34 patients where 0.75 per cent solution was used, and 14.2 per cent in 28 patients where 1.0 per cent solution of Viadril was administered, for an over-all average of 7 per cent. From table 1 it is seen that dosage also increased with percentage of solution. We must assume that the percentage of thrombophlebitis is proportional to strength of solution used rather than just increase in dosage alone. There, however, may be some correlation between the two.

DISCUSSION

The use of a steroid for the production of general anesthesia opens up many new avenues of thought as well as the possibility of a new series of allied compounds. Certainly in so far as intravenous anesthetic agents are concerned this is the first new approach that has been presented.

In most respects this drug differs very little clinically in its production of systemic depression from the thiobarbiturates. If the latter group of drugs are used in concentrated solutions and in large dosage many phenomena may be ascribed to them. Endotracheal intubation may be accomplished with thiobarbiturates alone if the patient is grossly overdosed and depressed sufficiently; some skeletal muscle relaxation may be produced in the same manner. Only small supplemental doses of other agents are necessary to prolong the general anesthesia that has been induced by an overwhelming initial dose of the thiobarbiturates. Further we know that systemic blood pressure will suffer a precipitous decline and spontaneous respirations will become a nonentity following too large a dose of a thiobarbiturate administered too rapidly. It is our opinion that if just enough Viadril is used intermittently or continuously to produce the desired level of "anesthesia" and if this is prepared in 0.5 per cent concentration or less, many of the undesirable circulatory and respiratory responses can be eliminated.

Viadril seems to have one distinct advantage, the absence of laryngospasm. Confusion and disorientation in the older age groups, so commonly seen after the use of thiobarbiturates, was singularly absent.

The incidence of thrombophlebitis is a distinct deterrent to the accepted use of this drug at present. There seems to be (table 4), a distinct correlation between thrombophlebitis and concentration of solution. This factor can certainly be minimized by using more dilute concentrations, and by administering the drug into a large vein whose flow is unobstructed.

The lag time in producing anesthesia is not particularly disturbing to us, however, where one is pressed for time it certainly becomes a factor to consider.

SUMMARY

Viadril, 21-hydroxypregnanedione sodium succinate, was administered intravenously to 114 patients undergoing a wide variety of surgical procedures. Clinical observations indicated that Viadril produced hypnosis to a rather predictable degree. Complications of Viadril administration included hypotension, respiratory depression and thrombophlebitis. A clinical comparison of the effects of concentrations of Viadril in 0.5 per cent, 0.75 per cent, and 1.0 per cent points to the fact that as the concentration and dosage increase, so do the undesirable complications.

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BRACHIAL PLEXUS BLOCK: A RE-EVALUATION AND A PROPOSED APPROACH

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Despite recent advances in general anesthesia, regional block anesthesia still remains one of the most important weapons in the armamentarium of the anesthesiologist. There are several reasons for this. First, it is the type of anesthesia which causes the least physiologic disturbances. Second, regional block many times is ideal for emergency surgery for trauma. Patients with acute traumatic conditions often have a full stomach or invariably have food retained in the stomach due to reflex pyloric spasm. Under general anesthesia vomiting and aspiration still ranks as one of the most important causes of anesthetic death. Use of regional block apparently will avoid or minimize these catastrophes.

However, regional block is not without its limitation and disadvantage. For instance, for surgery of the lower extremity, to employ regional block one has to block the sciatic, femoral, lateral femoral cutaneous and obturator nerves. This is not only very time consuming but many times is unsuccessful. For surgery of the upper extremity below the shoulder joint, the situation is different. One of the most useful, simple and satisfactory methods in the field of regional anesthesia is a block of the brachial plexus.

Halsted in 1884 operated upon the upper extremity under brachial block produced by the injection of cocaine into the root of the neck. Crile in 1897 infiltrated the skin supraclavicularly with cocaine and exposed the brachial plexus by incision. He then injected cocaine directly into the nerve roots and performed a shoulder disarticulation without much difficulty. In 1911 Hirschel injected the brachial plexus by the axillary route and Kulen Kampff approached it from above the clavicle. Both of them did their injections blindly without definite landmarks and their results were not predictable. Since then there have been described the posterior paravertebral approach by Kappis and the infraclavicular technic by Louis Bary. All of these, except the supraclavicular technic, have fallen into disuse, due to their complexities and inaccuracies.

Although the supraclavicular technic is still widely employed, the rate of success by the experienced hand before 1940 was only 60 to 80 per cent. J. Patrick⁵ in 1940 reviewed the subject and described his modified supraclavicular technic. He used the midpoint of the upper border of the clavicle as the bony landmark, inserted his needle right above the upper border of the clavicle at this point and directed it toward the second and third dorsal spine. When he touched the first rib he injected planocaine and withdrew the needle to the subcutaneous tissue. He repeated this injection 6 or 7 times, each time directing

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the needle 5 mm. nearer the sternal end until he was close to the subclavian artery. He used a total of 60 to 70 cc. of 2 per cent planocaine. He claimed only 1 failure in 44 cases.

This technic has several disadvantages. It is time consuming; it is not an anatomic block in the true sense; it is too easy to puncture the subclavian artery; it necessitates the use of 3 or 4 times more local anesthetic agent than necessary, therefore increasing the hazard of toxic reaction; and last, the repeated injections may increase the chance of nerve damage.

In reviewing the literature on regional anesthesia^{1, 2, 3, 4, 5, 6, 7, 8} the technics for supraclavicular brachial plexus block can be summarized and outlined as follows:

1. These authors employ the subclavian artery, midpoint of the clavicle, external jugular vein and scalenus anticus muscle as landmarks and agree that the subclavian artery is the most reliable one.

2. The needle is inserted variously from 1 cm. to 2 cm. above the clavicle, invariably directed backwards, inwards and downwards toward the second and third thoracic vertebrae.

3. They claim that best results will be obtained when the needle impinges on the nerve and the patient develops paresthesia radiating down the arm. After several trials, if no paresthesia is obtained, Patrick's technic⁵ should be employed.

4. Positioning of the patient is emphasized. The patient's shoulder, on the side to be injected, should be lowered as far as possible so the position of the plexus as it crosses the first rib will not be covered by the clavicle.

When we first started to use the conventional technic 3 main difficulties were encountered. We failed to obtain a successful block from time to time. Many times the subclavian artery was entered and embarrassing bleeding was encountered. The fear of producing pneumothorax was ever present. These difficulties stimulated us to re-evaluate the technic. Our study started with cadaver dissection and followed with clinical trial and analysis.

CADAVER DISSECTION

Method: In the first group, consisting of 10 cadavers, needles were inserted approximately 1 cm. above the midclavicular point according to the conventional method. Five cc. 1 per cent methylene blue was injected each time the needle touched the first rib and when the needle was withdrawn from the rib. In 10 other cadavers we used a modified technic. The needle was inserted about 1 cm. above and about 1 cm. medial to the midclavicular point; the direction of the needle was backward, downward, and outward, instead of inward. The same amount of methylene blue was injected as in the first group (fig. 1, A & B).

Findings and Results: Dissection of the brachial plexus region was carried out after the injection of methylene blue. Several important anatomic facts pertaining to blocking the brachial plexus were revealed on these dissections.

The brachial plexus is enveloped in a fascial compartment. The fascia is derived from that covering the scalenus medius and scalenus anticus muscles.

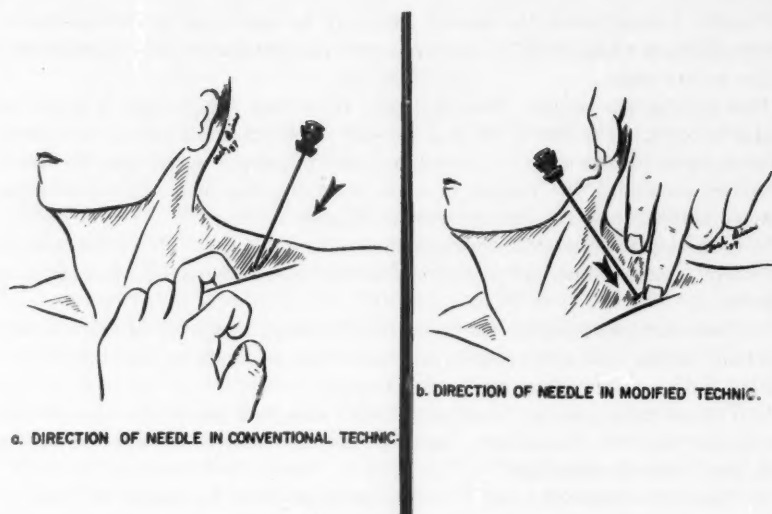
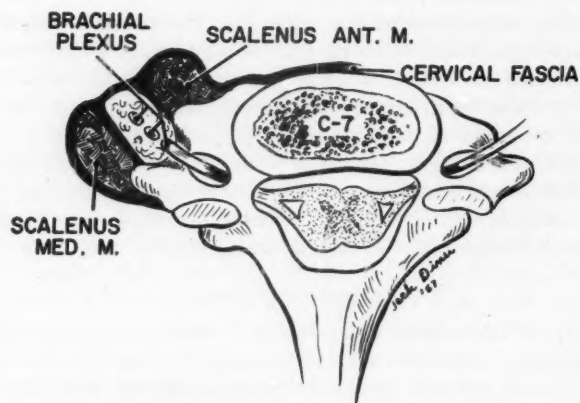


FIG. 1



CROSS SECTION DEMONSTRATES THE FASCIAL COMPARTMENT OF THE BRACHIAL PLEXUS.

FIG. 2

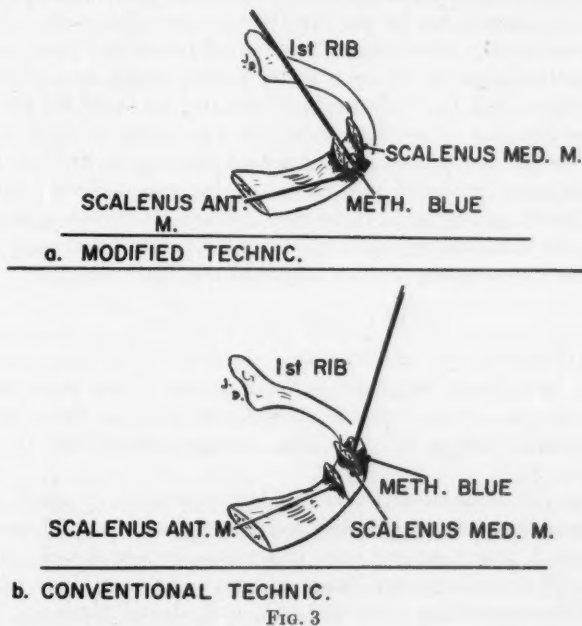
Medially it is continued as prevertebral fascia (fig. 2). This is important because the brachial plexus will be affected only when the anesthetic agent is injected inside this fascial compartment.

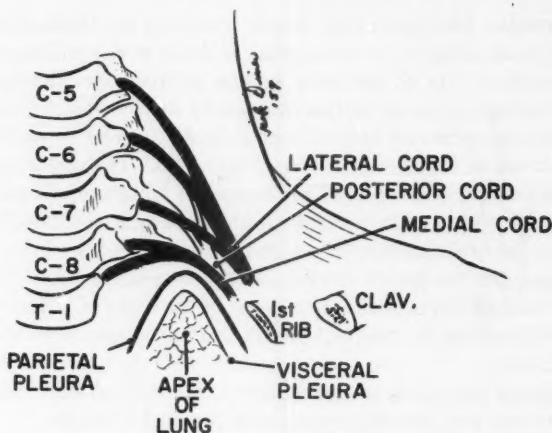
The part of brachial plexus which concerns us is the portion on the first rib, which was found to vary from 2 to 3 cm. in length and from 1.8 to 2.8 cm. in width. The other part of the plexus, even though we may puncture it accidentally, is of no practical value because we have to rely on the first rib to determine the

depth of the needle. The upper and middle trunks of the brachial plexus, from the dissection of 20 cadavers, invariably lay in front of the scalenus medius and only the lower trunk lay in the bony groove between the attachment of the scalenus anticus and scalenus medius muscles to the first rib. (The area of the groove between the scalenus anticus and scalenus medius is smaller; varying between 1 to 2 cm. in length and 1.8 to 2.8 in width.) The scalenus medius was inserted in the first rib in an oblique line instead of a horizontal line from medial to the lateral side (fig. 3). The subclavian artery is located immediately medial and inferior to the brachial plexus and usually in front of the lower trunk. The apex of the lung and the pleura extend into the root of the neck, reaching from 2.5 to 4 cm. above the level of the sternal end of the first rib. This extension as a rule is mediosuperior to the brachial plexus and medioinferior to the subclavian artery (fig. 4).

A fatty tissue or areolar tissue pad about 3 to 4 mm. in thickness intervened between the trunks and the rib, especially in the husky patient.

The distance between the upper edge of the clavicle to the middle trunk at the midpoint of the first rib of the 12 cadavers under 5 feet 6 inches averaged .9 cm., of the 8 cadavers with height more than 5 feet 6 inches the average distance was 1.2 cm. In 90 per cent of the 20 dissections the midclavicular point corresponded to that point at which the middle trunks of the plexus go under the clavicle. The external jugular vein or its extension beneath the clavicle varied from 1 cm. to 2.5 cm. from the midpoint of the clavicle in 80 per cent of cases.





DEMONSTRATING THE APEX OF THE LUNG

FIG. 4

Therefore the reliability of the midclavicular point as a landmark, is only secondary to the subclavian artery. The external jugular vein cannot be used as a reliable landmark.

In addition to the above anatomic facts, we discovered some other interesting findings in our dissections. In the first 10 cadavers that were injected with methylene blue by the conventional technic, we found in 6 cases most of the dye was deposited posterior to the scalenus medius muscle and between it and the first rib (fig. 1, A & B). In 2 cases we found the dye inside the pleural cavity at the apex and medial to the first rib. In only 2 cases did we get enough deposition of dye around the trunks of the brachial plexus over the first rib. In the second 10 cadavers we found in 6 cases the dye was deposited satisfactorily around the trunks, mostly around the middle trunk. In 3 cases most of the dye was deposited behind the trunks in the fatty tissue. In 1 case most of the dye was inside the pleural cavity but lateral to the first rib.

CLINICAL TRIAL AND ANALYSIS

From the dissections we concluded that the modified technic, as used on the second group of cadavers was more rational, at least it was more anatomically sound than the conventional method. In order to prove its merits we used this technic for clinical trial on 137 cases (this number includes only those done by the authors).

Method: All patients were given the usual premedication for adults, most often 100 mg. meperidine, 0.4 mg. atropine, and sometimes 100 mg. of pentobarbital. The usual block tray used consisted of various sizes of 3 inch, 20-22 gauge needles; one 20 cc. syringe; one 10 cc. syringe; one 5 cc. syringe. One per cent lidocaine with epinephrine 1:100,000 was used almost routinely. This agent

gave us a more profound and longer lasting block; also it seemed to have some sleep inducing properties. In hypertensive patients an aqueous solution of lidocaine without epinephrine was used. The amount of drug varied from 20 to 40 cc. The volume injected depended upon the type of surgery contemplated and upon the estimated time for the procedure. We never exceeded 500 mg. of drug for any patient.

We positioned the patient in the usual way making sure the patient's shoulder was not elevated. The angle formed by the sternal end of the clavicle with the horizontal line we called C angle. In a survey of 100 ward patients in the standing position, the angle averaged 20 degrees. Patients, due to trauma of upper extremity etc., often elevated the shoulder and the angle sometimes was found to be about 30 degrees. Any increase in the angle above 20 degrees will only make identification of landmarks more difficult.

If the patient's height was below 5 feet 6 inches, a 22 gauge block needle was inserted about 1 cm. above the clavicle. If the patient's height was above 5 feet 6 inches, the needle was inserted about 1.5 cm. above the clavicle.

If the subclavian artery could be palpated, the needle was inserted just lateral to it and directed downward, backward and outward. In about 58.8 per cent of the patients in our series the subclavian artery could not be palpated. In the other 41.2 per cent where the subclavian artery could not be felt, the needle was inserted about 1 cm. medial to the midclavicular line.

In an average patient it was necessary to insert the needle to the depth of 3 to 3.5 cm. in order to touch the first rib, but in a heavy patient it was necessary to insert the needle to a depth of 5.5 cm. before it encountered the first rib. In an average patient it was found that if the needle went beyond 3.5 cm., it was most probable that the needle would touch the posterior portion of the first rib and injection would be ineffective and dangerous. When the needle touched the first rib paresthesia might be elicited, if so, the needle was fixed at this point and 5 cc. of solution injected, slowly withdrawing the needle until another 10 cc. of solution was injected. Prior to injection, of course, aspiration was carried out in order to be reasonably sure that the needle point had not entered a blood vessel. After the needle had been withdrawn to the subcutaneous tissue it was reinserted directly downward and backward until the first rib was encountered again, then the same procedure of injection was carried out. By this manner sufficient anesthetic agent is deposited around the lower trunk to insure an adequate block.

Results: A brief analysis of the 137 cases. Patients' age varied from 14 to 86 years. Operations varied from reduction of Colles fractures to extensive open reductions, repair of extensive lacerations, tendon repairs, and nerve repairs. Duration of operations were from 15 minutes to 3 hours and 40 minutes. In 90 per cent of the patients, a tourniquet was used without complaint of pain.

In 130 patients out of 137 we elicited paresthesia before injecting the anesthetic agent. In 5 of the other 7, we had to infiltrate the area more or less in the manner of Patrick's technic except the needle was inserted outward instead of inward. In 135 patients we had good results. We failed in 2 patients. One was

a patient with Klippel Feil syndrome in whom we believe we never located the plexus. The second case was a psychiatric patient, who was totally uncooperative and a poor candidate for this type of procedure.

There were no cases of pneumothorax in the entire series of cases detectable by physical examination or by symptoms. Thirty-six patients had routine chest roentgenograms postoperatively, and no signs of pneumothorax were seen. Minor bleeding occurred in 10 per cent of the patients. Ninety per cent of the patients slept throughout the surgery without supplementing their usual pre-medication.

SUMMARY

By anatomic dissection, and clinical application, a modified technic for brachial block which differs from the conventional supraclavicular method is presented. The block needle is inserted 1 cm. above and 1 cm. medial to the midpoint of the clavicle, directly downward, backward and outward instead of inward. Anatomic dissections point out the important reasons for failure in doing brachial block. We have used this modified technic in 137 patients with only 2 failures and with no cases of proved pneumothorax.

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THE RELATIONSHIP OF A BILIARY LIPOPROTEIN "COMPLEX" TO SOME THEORIES OF GALLSTONE FORMATION*

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INTRODUCTION

Although our knowledge of the mechanisms of gallstone formation is primarily theoretical and fragmentary, few significant advances in our understanding of this process have been made in the past decade. Some recent interesting electrophoretic studies of bile have suggested new aspects concerning mechanisms of gallstone formation. Therefore it appears worthwhile to review briefly some of the theories of gallstone formation and to present some of the results of the recent electrophoretic studies along with a consideration of their possible significance.

COMPOSITION OF GALLSTONES

Cholesterol is the principle component of most gallstones. Under the microscope cholesterol appears in the form of clear, flat crystals with straight edges and often with a typical notch missing from one corner (fig. 1, right). In some instances gallstones may be composed almost entirely of cholesterol, in which case they are called "pure" cholesterol stones or cholesterol solitaires (fig. 1, left).

Pigment is the next most common component of gallstones, although its percentage by weight is relatively small because of its light molecular weight. Microscopically pigment usually appears in the form of amorphous yellow or orange granules of calcium bilirubinate (fig. 2, right). When these yellow or orange granules of pigment are massed together in a stone the color appears brown. As in "pure" cholesterol stones, pigment also is the chief component in "pure" pigment stones (fig. 2, left).

Most gallstones contain large amounts of cholesterol and lesser amounts of calcium bilirubinate pigment. Such calculi are known as "infectious" or mixed gallstones (fig. 3, left). Microscopic examination of scrapings from these infectious tones will show a mixture of cholesterol crystals and calcium bilirubinate granules (fig. 3, right).

Calcium carbonate, a third component, is found in a small percentage of gallstones and is the substance responsible for the unusually dense or "calcified" appearance of these calculi. Calcium carbonate may be precipitated on the outside of other types of stones, or it may be found distributed homogeneously within the amorphous or granular type of stone illustrated (fig. 4, left). Under the

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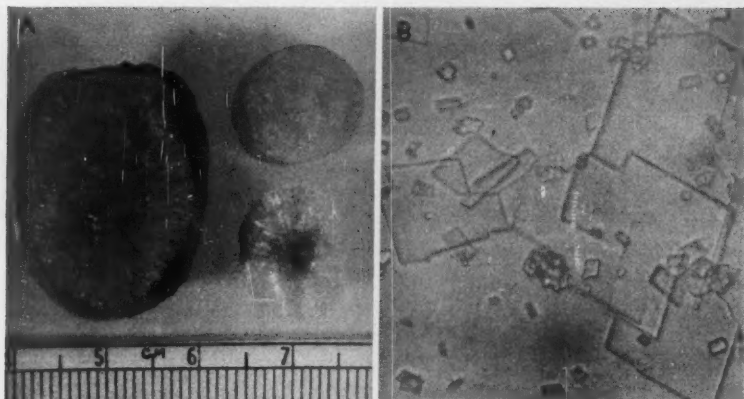


FIG. 1. "Pure" cholesterol gallstones. A: Cross sections of two different cholesterol solitaires. The stone on the right does have a pigment center but the remainder of the stone is composed of almost transparent cholesterol. The stone on the left has a thin outer mixed layer of cholesterol and pigment. B: Photomicrograph of typical cholesterol crystals under high power. Scrapings of gallstones pictured in "A" will show crystals like these. (Reproduced by permission of the publisher from *Gastroenterology* 32: 175, 1957, Fig. 2A, p. 198.²⁶)

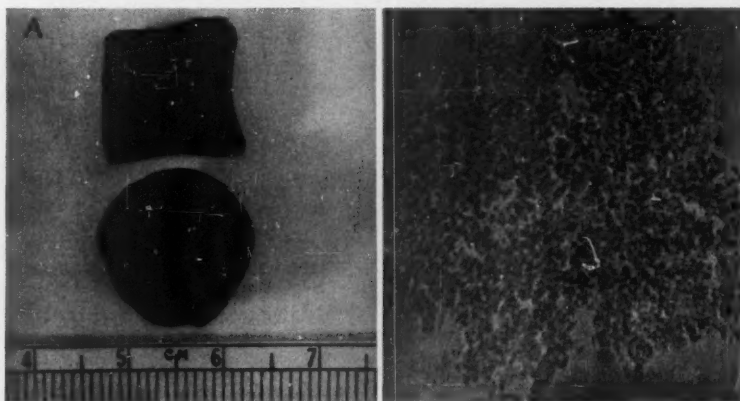


FIG. 2. "Pure" pigment bile duct stone. A: Cross section and outer surface of a "pure" pigment stone. This particular stone was removed from the intrahepatic bile ducts of a patient with chronic pyogenic cholangitis and made available by Dr. J. Cook, Hong Kong. B: Photomicrograph of a clump of yellow granules of calcium bilirubinate under high power. Most pigment stones contain pigment granules such as these. (Reproduced by permission of the publisher from *Gastroenterology* 32: 175, 1957, Fig. 7B, p. 202.²⁶)

microscope scrapings from the calcified portion of such gallstones show crystals with strange shapes and alternating bands of green, yellow, brown and white (fig. 4 right). These crystals have been referred to as microspheroliths.²⁷

SOME THEORIES OF GALLSTONE FORMATION

The literature on gallstone formation is voluminous and almost impossible to review. Only theories which still appear plausible will be mentioned. Among

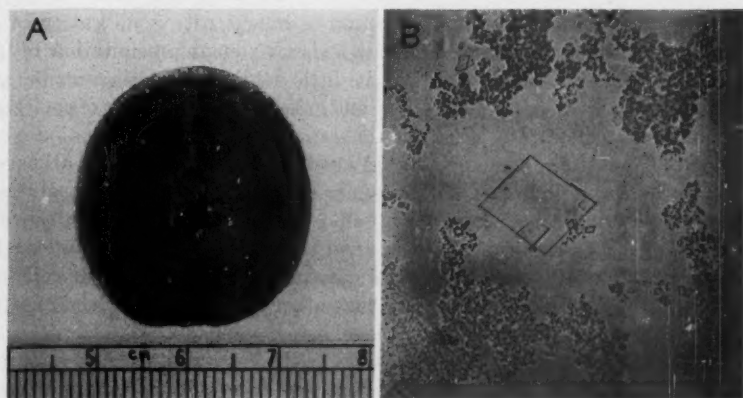


FIG. 3. Mixed or infectious gallstone. A: Cross section of a "mixed" gallstone showing alternating light and dark brown bands. This type of stone also is referred to as an infectious gallstone. B: Photomicrograph of clumps of yellow calcium bilirubinate pigment and cholesterol crystals under high power. Mixtures like this are found in scrapings of mixed gallstones. (Reproduced by permission of the publisher from *Gastroenterology* 32: 175, 1957, Fig. 7F, p. 202.²⁶)

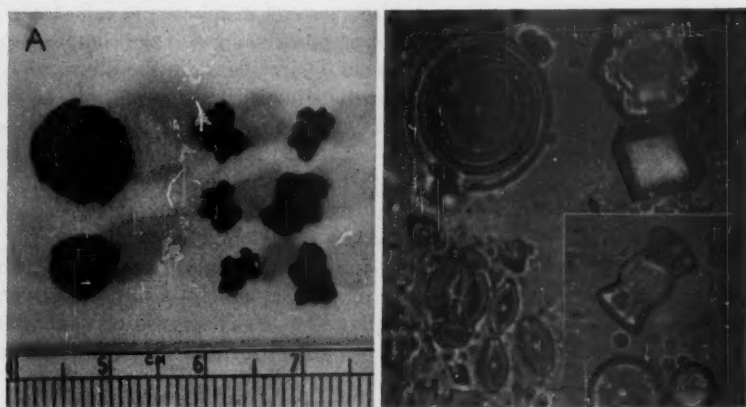


FIG. 4. Calcium carbonate-containing gallstones. A: Outer surfaces of two types of brittle, granular black homogeneous gallstones. They differ from the "pure" pigment stone because of their calcium carbonate content and they often are radiopaque or "calci-fied". B: Photomicrograph showing various forms of "microspheroliths" under high power. These crystals contain calcium carbonate and varying amounts of yellow, green or brown pigment. Often concentric laminae of varying colors can be seen, suggesting formation of minute "mixed" microcalculi. Scrapings of the stones pictured in "A" will contain such microspheroliths. (Reproduced by permission of the Editor from the *American Journal of Medicine* 20: 383, 1956, Fig. 2, p. 385.²⁷)

these theories are those dealing with stasis, infection, inflammation, protein alterations and colloidal phenomena of the biliary tract, intrahepatic bile duct nuclei and systemic metabolic changes.^{1-3, 7, 30-31, 34-36, 48, 50-51, 55}

Fernelius,⁷ in 1554, apparently was the first to relate gallstone formation to bile stasis from biliary ductal obstruction. In 1863 Thudichum⁵⁰ expanded the

stasis theory to include abnormal secretion of mucus with acidification of the bile, resultant decomposition of bile salts and subsequent precipitation of cholesterol and pigment. Today there can be little doubt that stasis contributes to stone formation. Frequently microscopic and grossly visible crystals of cholesterol and clumps of pigment are found in bile trapped behind an obstruction of the common bile duct from carcinoma of the head of the pancreas in the absence of significant inflammation. In a few instances of this type where the obstruction was prolonged, tiny calculi have been found in the gallbladder. Usually stones forming chiefly as a result of bile stasis will have a high pigment content. The relative importance of stasis in the formation of the usual type of gallstone, however, is not clear. It would appear that other factors are involved and that stasis probably is of secondary importance.

Infection of both the gallbladder and liver has been thought to be an important cause of gallstone formation since Gallippe's work in 1886.⁷ Naunyn, Aschoff and Bacmeister are names most often associated with this theory.^{1-3, 35} More recently others have attempted to induce gallstone formation in experimental animals by bacteriologic means.^{15, 30, 45} It was believed that bacterial inflammation of the gallbladder caused selective absorption of bile salts, leaving behind cholesterol and thereby upsetting the bile salt:cholesterol ratio. This ratio is important since the bile salts help hold cholesterol in solution in bile. Infection in the liver and bile ducts also is said to promote changes in the composition of bile and favor gallstone formation. One can find evidence in the literature both for and against the importance of infection in gallstone formation. In most cases it is difficult to prove that bacterial infection is present in the gallbladder or that it initiated formation of the calculus. Inflammation, especially non-bacterial, undoubtedly can contribute to stone formation. This is well demonstrated by formation of stones in the hepatic bile ducts of many patients with chronic cholangitis.¹² The greatest problem concerning the significance of inflammation of the gallbladder in stone formation, however, is whether or not the inflammation precedes calculus formation or merely occurs secondary to chronic irritation from the presence of the stone. The cause of nonbacterial inflammation of the gallbladder usually is obscure if it does precede gallstone formation.

Naunyn described the nucleus theory in 1896.³⁵ He had observed nuclei formed by epithelial cells, bacteria, protein or bile thrombi in the centers of gallstones and he believed these nuclei originated in the intrahepatic bile ductules. The presence of these nuclei in the gallbladder were believed to be the initiating factor in gallstone formation. It is true that a small pigment center or "nucleus" can be demonstrated in many gallstones. However, it is difficult to prove that such pigment centers arise in the intrahepatic bile ducts.

The metabolic origin of gallstones was described by Naunyn, Aschoff and Bacmeister.^{1-3, 35} This theory can be applied to both cholesterol and pigment "pure" stones. Since gallstones of high pigment content are associated with approximately 50 per cent of patients with chronic hemolytic anemias, it has been assumed that the excessive excretion of pigment causes supersaturation of bile

and pigment stones precipitate. This probably is the only situation where we really have a single acceptable mechanism for gallstone formation. Even here, though, the process probably is more complicated than it appears. Simple supersaturation of bile with pigment does not explain the presence of appreciable amounts of calcium carbonate in many of these stones, and it does not explain the presence of oxidized forms of bile pigment. Recent studies of the manner in which the liver handles bile pigment suggests that parenchymal liver cell damage and perhaps defective conjugation of pigment may play a part.^{4, 10-11, 21}

The "pure" or metabolic cholesterol stone has been thought to be the result of increased excretion of cholesterol into bile, either by way of the liver or through the gallbladder mucosa.^{3, 16, 17} Increased dietary intake of fatty substances and hypercholesterolemia were believed to be important factors.⁶ Statistical evidence of an increased incidence of gallstones in association with diabetes mellitus, hypothyroidism, obesity and pregnancy was assumed to support this contention since these conditions often were associated with hypercholesterolemia.^{32-33, 41} However, a direct relationship between stone formation and these conditions has not been demonstrated. Recent studies with C¹⁴-cholesterol and attempts to correlate bile cholesterol content with serum levels have shown no relationship of blood cholesterol to bile cholesterol.^{19-20, 23-25, 43-44} In fact, there is reason to believe that the largest portion of cholesterol passing from the blood to bile is converted by the liver to bile salts. Theoretically this should increase the ability of the bile to hold cholesterol in solution, and not cause precipitation of cholesterol. Although cholesterol stones have been induced in experimental animals by special diets, there is no direct evidence that diet causes gallstone formation in human beings.^{8-9, 13, 18, 22} The correlation between cholesterosis of the gallbladder and formation of "pure" cholesterol gallstones is too poor to indicate any definite relationship. One is forced to conclude that little is known about the mechanism of formation of cholesterol solitaires.

The electrical charge theory was proposed by Lichtwitz in 1908.³¹ He, as well as others,^{5, 14, 49} noted an increase in biliary protein in many patients with cholecystic disease. Lichtwitz believed that bile cholesterol was held in colloidal solution because of negative charges on the particles. The increased protein content of bile from diseased gallbladders probably was the result of mucosal inflammation. Since the particles of protein carried a positive charge, their presence in large numbers neutralized the negative charge on the cholesterol particles. This neutralization permitted the particles of cholesterol to agglutinate and crystallize. This was thought to result in formation of calculi. Protein may indeed be an important factor in gallstone formation, but more recent work has suggested that the mechanism involved is entirely different from that proposed by Lichtwitz.

The Liesegang phenomenon, often expounded by Sweet⁴⁶⁻⁴⁷ and Kleeberg,²⁸⁻²⁹ is used to explain the concentric layers of pigment seen in the mixed type of gallstone. This theory is an application of a colloidal phenomenon readily demonstrated in models. Presumably a colloidal plastic mass of cholesterol and calcium ions forms within the gallbladder and is molded into the shape of the stone or

stones which will form. As pigment penetrates the plastic mass from the periphery it combines with the calcium to form insoluble calcium bilirubinate. The precipitation of this insoluble pigment occurs in a rhythmic fashion, leaving intervening bands free of pigment. Precipitation of calcium upsets the colloidal system and cholesterol crystallizes out in the spaces where pigment is absent. While this theory can be demonstrated readily in models, it is difficult to accept this as the chief mechanism of gallstone formation. Such transient plastic masses have not been found within gallbladders by chance at operation or at autopsy. Experience suggests that the process of stone formation takes place over a relatively long period of time, although probably intermittently, and not in the course of several hours as in the model. It is possible, however, that an individual layer might be deposited on a forming gallstone by a chemical process similar to the Liesegang phenomenon.

Calcium carbonate appears to be deposited in gallstones by special mechanisms. There is considerable correlation between cystic duct obstruction and deposition of calcium carbonate on the surface of stones.^{37-40, 42} It is believed that calcium is excreted by gallbladder mucosa in the presence of a certain degree of inflammation and cystic duct obstruction. In these instances the calcium carbonate is deposited on the surface of stones present in the gallbladder. Calcium carbonate also can be found distributed homogeneously throughout other types of stones, especially those secondary to chronic hemolytic anemia. The source of the calcium carbonate in this type of stone is obscure. In addition, in liver disease or chronic hemolytic anemia hepatic bile may contain calcium carbonate-containing microscopic crystals known as microspheruliths.²⁶

PAPER ELECTROPHORETIC STUDIES OF BILE

In 1956 Verschure and associates⁵²⁻⁵⁴ published three articles presenting the results of their studies of bile. Similar studies utilizing the paper electrophoretic technics reported by this group are in progress in our laboratory and in general our results appear similar*. A 0.02 to 0.04 ml. sample of bile is placed on filter paper strips in a Spinco electrophoretic cell with a barbital buffer of pH 8.6. The strips are submitted to an electrical field of approximately 7.5 V/cm. for 3 hours and then dried. The dried strips are stained with bromphenol blue to identify protein and with Sudan black to identify lipids. Bile pigments can be recognized without staining because of their natural color.

Figure 5 illustrates the electrophoretic pattern found in normal gallbladder bile. Strips showing the location of protein, lipid and pigment are included. Normal gallbladder bile has a single dominating protein, lipid and pigment band which are labeled P₁, L₁, and B₁ respectively. In some instances a second pigment band, B₂, is present.

Figure 6 represents a pattern obtained from abnormal bile. A definite residue of protein and lipid can be seen at the point of application of the specimen. The same single band of protein, lipid and pigment are present, as in figure 5, but

* Mrs. Eleanor Crabtree, Dr. Eugene T. Hansbrough and Dr. Clarence L. Chester are assisting in this study.



FIG. 5. Electrophoretic patterns in normal gallbladder bile. This figure shows three paper electrophoretic strips obtained from a sample of normal bile aspirated from the gallbladder at operation. The upper strip was stained with bromphenol blue for protein, the middle strip with Sudan black for lipid, while the bottom strip is unstained so that pigment will be visible. The vertical lines represent the point of application of the bile sample and the direction of migration is from left to right. The bands P_1 , L_1 , and B_1 represent the molecular complex found in normal gallbladder bile. These bands are not found in hepatic bile. In a few instances a second pigment band, B_2 , was found in normal gallbladder bile.



FIG. 6. Electrophoretic patterns in abnormal gallbladder bile. This figure shows three paper electrophoretic strips obtained from a sample of bile aspirated from a gallbladder showing minimal cholecystitis but containing gallstones with a high cholesterol content. The bands P_1 , L_1 , and B_1 , although present normally, are unusually dense and represent an apparent increase of the lipoprotein complex above normal. This is not the most common finding in abnormal bile. A faint second protein band, P_2P_2 , is apparent and there is residue at the point of application of the bile sample.

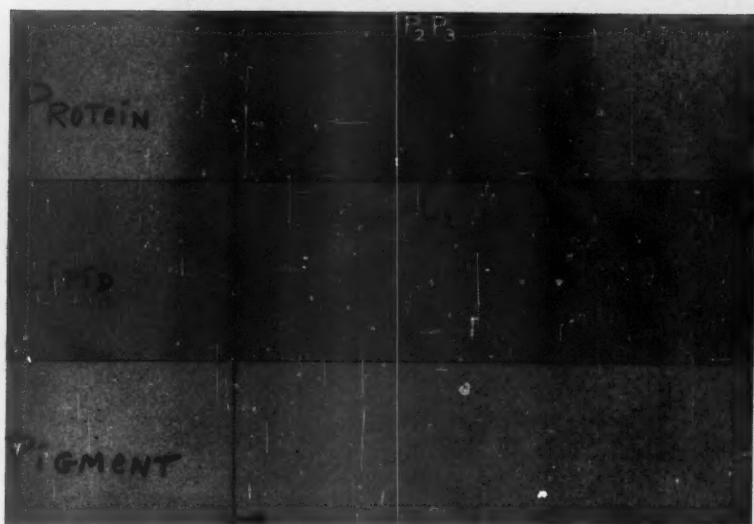


FIG. 7. Electrophoretic patterns in abnormal gallbladder bile. This figure shows three paper electrophoretic strips obtained from a sample of bile aspirated from a gallbladder showing cholecystitis but not containing gallstones. The P_1 , L_1 , and B_1 bands are greatly reduced or absent, the more common finding in abnormal bile. A second dense protein band, P_2P_3 , which resembles albumin has appeared. A third protein band, P_4 , which is believed to be mucin is faintly visible.

here the density of these bands is increased considerably above that found in normal bile. This increase is not a common finding but is one of the alterations sometimes seen in bile from diseased gallbladders.

Figure 7 illustrates the electrophoretic pattern more commonly seen in bile from diseased gallbladders. Here the P_1 , L_1 , and B_1 bands normally found are greatly reduced and the dominating protein band, P_2P_3 , now is located behind P_1 . A third protein band, P_4 , also has appeared near the point of application.

Figure 8 summarizes diagrammatically the data obtained from the electrophoretic studies of bile. It can be seen that one normally finds protein, lipid and pigment from gallbladder bile located in one area. This suggested the presence of a single component containing protein, lipid and pigment. Verschure and his associates^{52, 54} carried their studies further, using free electrophoresis, ultracentrifugation and chemical studies. They found that a complex was present in gallbladder bile. The nucleus of this complex was a lipoprotein containing lecithin and polypeptides. About this nucleus were attached cholesterol, lipid, pigment and even bile salts. The molecular weight of the complex was not constant and various components could be split off by different procedures. Therefore the "bonds" holding the complex together probably were loose ones. This complex was found in normal gallbladder bile, was absent in hepatic bile and often was reduced or absent in bile from diseased gallbladders. Therefore it appeared that the lipoprotein was secreted by the gallbladder mucosa. Studies of macerated gallbladder mucosa did show the presence of a similar lipoprotein.

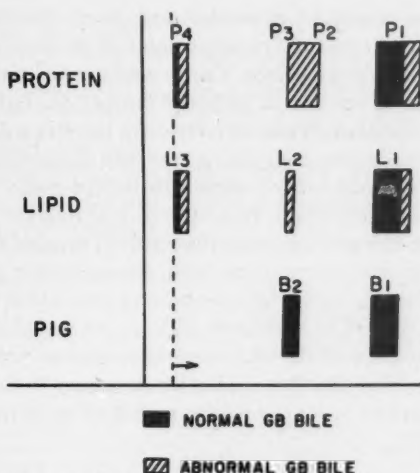


FIG. 8. Diagrammatic representation of the electrophoretic patterns found in normal and abnormal gallbladder bile. Paper electrophoretic patterns for protein, lipid and pigment are shown in diagrammatic fashion. The black blocks represent the location of normal bands, while the shaded portions represent the abnormal bands. The vertical broken line indicates the point of application of the sample and the direction of migration is from left to right. The P₁, L₁, and B₁ bands are in the area where the lipoprotein complex is located. As indicated, the lipoprotein complex occasionally is increased in disease but more often it is reduced or absent. Inflammation of the gallbladder, usually associated with the presence of stones, causes a band of protein resembling albumin to appear in the P₂P₃ area. In some cases lipid has appeared in this area at the same time, suggesting the possibility of a second type of lipoprotein in disease. The P₄ band is believed to represent mucin and is located just in front of the residue at the point of application.

DISCUSSION

If further investigation confirms these electrophoretic findings, we now have a more adequate explanation of the part played by protein and lipid in gallstone formation. At the present time it appears that gallbladder mucosa secretes a lipoprotein which serves as a complexing substance to hold pigment and cholesterol in solution while bile is being concentrated. Disease of the gallbladder decreases the secretion of this lipoprotein, thereby reducing the stability of bile and favoring gallstone formation. In addition, abnormal proteins resembling albumin (P₂P₃) and mucin (P₄) appear in bile. These abnormal proteins probably come from altered secretion or from exudation of blood or serum from the gallbladder mucosa, and they in turn also may contribute to instability of the bile.

The belief that protein changes were important in gallstone formation is not new. As early as 1863 Thudishum⁵⁰ mentioned abnormal secretion of mucus, in addition to stasis, as a factor which altered the pH of bile and which was related to gallstone formation. Naunyn³⁵ mentioned protein as one of the substances which could form the intrahepatic bile duct nuclei which he believed initiated formation of infectious gallstones. One would assume that such protein arose from the bile duct area. Other investigators noted an increase in protein content of gallbladder bile in cholecystic disease.^{5, 14, 31, 49} Lichtwitz³¹ related this increase

in protein to gallstone formation in his electrical charge theory. In most of these instances just mentioned presence of large amounts of abnormal protein in bile was believed to be the primary defect. The recent electrophoretic studies do confirm the importance of protein in gallstone formation, but they suggest an entirely different mechanism. While an increase in the amounts of protein resembling albumin and mucin may well play a part, the *absence* of a lipoprotein normally present in gallbladder bile appears to be the more important protein mechanism in gallstone formation. In addition, it is difficult to be certain that much of the albumin-like protein is not the result of surgical trauma to the gallbladder during its removal at operation. Also, stones already present often cause small mucosal erosions through which serum and even blood may ooze into the bile prior to operation. It is extremely difficult to completely exclude these possible secondary sources of the abnormal albumin-like protein found in bile from diseased gallbladders. Further studies are necessary to elucidate the relative importance of the various types of protein, as well as lipid, found in gallbladder bile.

SUMMARY

The composition and some of the theories involved in the formation of the chief types of gallstones are reviewed briefly. A summary of some recent electrophoretic studies of bile is presented. The electrophoretic studies suggest the presence of a lipoprotein in normal gallbladder bile. This lipoprotein is not found in hepatic bile and it often is reduced or absent in gallbladder bile in cholecystic disease. This lipoprotein appears to form a complex with cholesterol and pigment, thereby helping maintain these substances in solution. The absence of this lipoprotein appears to be an important factor in formation of at least the common variety of gallstone. Insufficient information is available to determine if this lipoprotein complex is an important factor in formation of other types of gallstones.

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OBSERVATIONS ON THE TREATMENT OF A STERILE, LETHAL
FORM OF EXPERIMENTAL ACUTE PANCREATITIS*

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Although various therapeutic agents have been previously evaluated in experimental canine hemorrhagic pancreatitis, an objective assessment has rarely been made regarding the presence of infection or its significance in such studies. The basic importance of this consideration is evident in the light of the observation that the death of dogs from acute pancreatitis caused by the forceful injection of bile into the accessory pancreatic duct can be completely or largely prevented by the administration of various antibiotics.^{11, 12} Thus, a prerequisite in the execution of certain experiments on acute canine pancreatitis is the recognition and prevention of the susceptibility of dogs under adverse conditions to fulminating infections. Hara and associates,⁶ have described a method of producing a sterile yet highly lethal form of acute hemorrhagic pancreatitis. The mortality was 87 per cent in 16 of 23 dogs which fulfilled the criteria of a "sterile" pancreatitis. The comparative value of four modes of treatment has been studied in a group of 68 animals afflicted with hemorrhagic pancreatitis in this manner, the agents comprising: an antitryptic substance, (soybean inhibitor, Antitrypsin)‡ transfusions of whole blood, dextran (Plavolex)§ and a combination of blood and the soybean inhibitor. In addition, a comparative study of serum amylase and antithrombin levels and the antitryptic and tryptic activities of the serum was carried out.

Methods: Acute hemorrhagic pancreatitis was produced by a method previously described.⁶ Briefly, the technic consisted of the injection of 180,000 to 300,000 units of trypsin (Tryptar)¶ under extreme pressure into the accessory pancreatic duct of healthy mongrel dogs which had received 1.5 to 3 Gm. of oxytetracycline hydrochloride (Terramycin) and neomycin|| orally for 3 to 4 days preceding operation. Bacteriologic examination of the stools obtained before operation and pancreatic tissue excised at operation was performed routinely. Immediately following production of the pancreatitis, the therapeutic agent of choice was administered over an 8 to 12 hour period. In addition each animal received .2 to .4 Gm. oxytetracycline intramuscularly in the postoperative period.

In all animals which had died, cultures of the peritoneal fluid, pancreas, gall-

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‡ The Antitrypsin, which was supplied by Dr. E. Loomis of Parke, Davis & Company, had antitryptic activity of 14.9 units per mg.

§ The Plavolex was supplied by Mr. S. Frank Messina of Wyeth Laboratories.

¶ The Tryptar was provided by Dr. Emil Fullgrabe of Armour Laboratories.

|| The Terramycin was donated by Dr. Harry Seneca and Dr. H. W. Rudel of Pfizer Laboratories, and the neomycin by Dr. Harold R. Reames of Upjohn Company.

TABLE I
Mortality of treated and untreated dogs with trypsin pancreatitis

	Number of Dogs	Mortality	Number of Sterile Pancreatitis	Mortality in Sterile Pancreatitis
Controls (saline).....	23	21	16	88%
Soybean Inhibitor (SBI).....	12	9	7	70%
Inactivated Soybean Inhibitor.....	4	3	3	75%
Dextran.....	19	14	14	74%
Blood.....	21	7	6	29%
Blood and SBI.....	12	4	1	11%

bladder bile and blood from the portal vein were immediately obtained. Determinations of the volume and hematocrit of the grossly bloody peritoneal exudate and grading of the severity of the pancreatic process were performed.

Blood amylase concentrations were measured by a modification of Somogyi's¹⁵ starch hydrolysis method and the serum antithrombin titers according to the technic of Innerfield.⁹ The antitrypsin activity of the serum was determined by the method of Wells and associates¹⁷ in the initial phase of the study and subsequently by a modification of the method of Anson and Mirsky.¹ A modification of the latter method was adopted for determination of the serum tryptic activity.

Control Group: The clinical course and pathologic findings in trypsin-induced pancreatitis have been described in a previous communication.³ The usual course was one of progressive shock terminating in coma and death after an interval averaging 10 hours. The pancreas at necropsy was a friable and swollen dark purplish-red mass, resembling, in the main, large blood clots. The peritoneal cavity contained 500 to 1000 cc. of bloody fluid with a hematocrit value of 5 per cent to 10 per cent. The over-all picture contrasted strikingly with the more benign process in bile-induced pancreatitis. Only those experiments in which the tissues and fluids secured at postmortem examination proved free of bacteria on culture were classified as "sterile".

Antitryptic Substance: The administration of an antitryptic material derived from soybean failed to improve the mortality or prolong the length of survival. A 2 to 4-fold prolongation of the clotting time was uniformly observed. The soybean inhibitor which was inactivated by autoclaving gave the same results as the active form.

Dextran (Plavolex): The comparative benefits of dextran and whole blood have been previously reported.⁸ Studies using radioactive globulin and dye T-1824 had revealed severe decrements in the blood and plasma volumes of 5 animals with trypsin-incited pancreatitis. The plasma expander provided little protection against the lethal effects of the pancreatic process despite the proved existence of profound hypovolemic shock. However, the average survival time was prolonged to 16½ hours. Serial measurements of the concentration of dextran in the serum demonstrated its disappearance from the blood stream at a more rapid rate in pancreatitis than in the control infusion. Concomitantly it ap-

peared in measurable amounts in the peritoneal cavity within an hour after induction of the pancreatitis. The administration of large amounts of dextran up to 60 ccl. kg. of body weight did not improve the mortality rate. The largest volumes of peritoneal fluid, totaling 1200 to 1500 cc. in some instances, were recorded in this group. A frequent complication in administering the plasma expander was the formation of large hematomas at the site of injection.

Blood Transfusions: The transfusion of whole blood in amounts of 35 to 45 cc. per kg. of body weight yielded not only a significant improvement in the mortality figures, but also an appreciable prolongation in the survival time. The surviving animals usually overcame the effects of the anesthesia within 4 to 5 hours and responded to stimuli a few hours thereafter. Of the 7 deaths, 2 occurred rapidly within $3\frac{1}{2}$ hours of a fulminating shock-state unresponsive to blood therapy. The remaining 5 lived on the average for 28 hours, more than double the survival time of the untreated animals.

Blood and An Antitryptic Substance: A combination of the two agents gave essentially the same mortality rate as in the previous category. Two animals died on the fourth and seventh days from generalized infection with *Clostridia*, an outcome that could have conceivably been prevented by more vigorous antibiotic therapy. The remaining dog died of *Escherichia coli* peritonitis and septicemia. Both the preoperative stool specimen and operative pancreatic biopsy in this instance yielded growths of this organism on culture, an infrequent occurrence in this study.

Antithrombin Titer: Innerfield⁹ has previously reported that an elevation of the antithrombin titer was a highly specific diagnostic aid in acute pancreatitis. A positive antithrombin test according to the criteria of Innerfield⁹ was obtained in only 11 of 58 animals with hemorrhagic pancreatitis. The plasma antithrombin level was evaluated in 68 experiments with multiple tests being run in 53. As many as 13 determinations were made over a 6 day period. There were 6 positive tests in 6 of 21 dogs (28 per cent) with pancreatitis produced by the bile injection technic compared with 5 positives of 37 (13 per cent) of the trypsin-induced series. The antithrombin activity was significantly elevated in 6 of 10 additional animals receiving an antitryptic agent.

Serum Amylase: The serum amylase level was measured simultaneously with the plasma antithrombin titer in 68 animals. The serum amylase was, with two exceptions, higher than the control value. There was extreme variability of the prepancreatitis amylase level, which ranged as high as 1200 units on two occasions. However, the amylase level in the 21 animals of the bile-pancreatitis were significantly higher than in the trypsin-pancreatitis animals. The great majority of the highest readings in the bile-pancreatitis group were at least triple the control level and increased an average of approximately 1700 units. In contrast, the elevation in most of the animals of the trypsin-induced lesion was twofold or less with the increments averaging 700 units.

Antitryptic and Tryptic Activities of the Serum: Serial determinations of the serum antitryptic activity were made in 18 experiments by the method of Wells and associates,¹⁷ and both the tryptic and antitryptic activities in 13 addi-

tional animals according to modifications of the technic of Anson and Mirsky.¹ The measurements were performed in animals belonging to two categories of bile-pancreatitis and three of trypsin-pancreatitis. The results obtained thus far were not consistent in any group tested. No characteristic patterns were observed which could be interpreted as reliably indicating the prognosis in a particular category. The majority of antitryptic titers determined by the method of Wells and associates¹⁷ were elevated 5 to 10 units after 2 to 4 hours. In the other series, the tryptic activity in most instances was elevated and the antitryptic activity proportionally decreased after 2 to 4 hours, but the pattern was not consistent.

DISCUSSION

The studies of Persky and associates,¹² are most significant in supporting the view that infection is the primary cause of death in bile-induced pancreatitis. Confirming the work of Dragstedt,³ Tower¹⁶ and others, these investigators have demonstrated the presence of bacteria, predominantly *Clostridia* and *Escherichia coli* in the pancreas, liver and other organs of healthy dogs. Bacteria, chiefly *Clostridia*, were found in the peritoneal fluid, pancreas and portal vein blood in the majority of dogs dying of pancreatitis incited by the injection of bile. The oral administration of chlortetracycline (Aureomycin) completely prevented death in pancreatitis in which the mortality had been 99 per cent in the control animals. Intravenous chlortetracycline,¹² penicillin,^{11, 12} polyvalent gas gangrene antitoxin¹¹ or neomycin were less effective. From the data they concluded that bacteria inhabiting the intestines were largely responsible for the virulent and usually fatal infection. Our results with oxytetracycline hydrochloride, although less impressive, reaffirmed the value of antibiotic therapy in bile-pancreatitis.⁶

The harmful effect of bacteria has been implicated in irreversible hypovolemic shock in dogs. Fine and his co-workers² have improved the mortality rate from 18 per cent to 88 per cent in their standard shock-producing experiments employing their bleeding method by the administration of chlortetracycline. A comparable magnitude of hypovolemia is present in experimental pancreatitis. Elliott¹ found that the loss in plasma volume in 6 dogs with bile-induced pancreatitis approximated 45 per cent after 8 hours. He has shown that the administration of 5 to 7 cc. per kilogram of concentrated human serum albumin yielded 10 survivors out of 15 animals with bile-induced pancreatitis. Likewise, 20 cc. per kilogram of 6 per cent Dextran resulted in the salvage of 4 out of 6 dogs. Thus adequate supportive shock therapy produced a significant decrease in the mortality. That the hypovolemic is by itself not of a critical degree is borne out by the previously mentioned effectiveness of certain antibiotics in experimental pancreatitis. The evidence presented would indicate that the incurrence of severe hypovolemic shock renders the untreated animal susceptible to an overwhelming infection and ensuing septic shock. It is imperative that future studies along these lines provide for an objective assessment of the element of infection, particularly when a comparison of the mortality rate is a factor.

The experimental lesion induced by trypsin is a more destructive and fulmi-

nating process than that obtained with bile. In trypsin-pancreatitis the swollen hemorrhagic pancreatic mass and the recovery of 500 to 1000 cc. of grossly bloody fluid from the peritoneal cavity indicate the loss of substantial quantities of blood which is greater than that in the lesion produced by bile. Measurements of the plasma and blood volume reveal that the decrements, particularly in the red cell mass, is more pronounced in trypsin pancreatitis.

The failure of an antitryptic substance of soybean origin in the treatment of pancreatitis confirms the results that Hoffman and his co-workers,⁸ Rush and Clifton¹³ and others¹ have previously reported. Although the use of a soybean inhibitor in 3 animals did not produce any survivors, Rush and Clifton concluded that it was of value in counteracting the shock found in pancreatitis in dogs. In this study the combination of an antitryptic agent and whole blood did not surpass the results obtained with blood alone. The data could be interpreted as reflecting some favorable influence on the part of the antitryptic substance, but the evidence was inconclusive.

The plasma expander, Dextran, failed to protect the dogs appreciably with trypsin-pancreatitis. The inability of dextran to maintain a critical expansion of the plasma volume is explainable on the basis of its ready leakage into the peritoneal cavity due to increased capillary permeability. The detailed data supporting this impression has been recorded in a previous communication.⁷ In addition, Davis and his group² have presented convincing evidence that dextran is unable to maintain the plasma volume in hypovolemia associated with increased capillary permeability. Adopting a standard thermal burn as a prototype of hypovolemia with increased capillary permeability, they demonstrated a fall of 59 per cent in the plasma volume and the loss of 70 per cent of the infused dextran from the circulation at the end of 4 hours. Our results with dextran are seemingly at variance with those of Elliott. However, the apparent discrepancy can be explained on the fact that a more lethal preparation of pancreatitis was employed in this study.

The superior results of treatment with blood over that with dextran suggests that a critical decrease in red cell mass is frequently present in trypsin-pancreatitis. The failure of blood transfusions to salvage an appreciable number of animals in this study would implicate other factors, besides hypovolemic shock and infection, in their death. In this regard there is no clear-cut evidence that so-called trypsin toxicity has any role in the demise of animals adequately treated with antibiotics and blood.

The serum amylase was far superior to the serum antithrombin titer in the diagnosis in experimental pancreatitis. Significant elevations in the serum amylase occurred more consistently in bile-pancreatitis than in the trypsin-induced process in which the rise was often negligible. This finding is not unexpected in view of the more destructive nature of the pancreatitis produced with trypsin and is in keeping with the clinical observation that the serum amylase is not infrequently only mildly increased in patients with the more severe forms of hemorrhagic or necrotizing pancreatitis.

Innerfield⁶ had reported that a significant elevation of the antithrombin titer

occurred in 50 of 55 patients with pancreatitis. The precise nature of the antithrombin complex is not known.¹⁴ The increase in the antithrombin activity has been ascribed to the release of proteolytic enzymes from the pancreas, although experimentally a decrease of the titer has been noted upon the intravenous injection of large amounts of trypsin.¹⁰ The poor correlation of the amylase and antithrombin test in this study may be due to the employment of trypsin as the inciting agent in the pancreatitis. The higher proportion of positive tests in animals receiving an antitryptic agent may be in support of this conclusion. However, the number of positive tests was still relatively low in the bile-pancreatitis group.

An attempt has been made to study the significance of proteolytic and antiproteolytic activities in experimental pancreatitis. Rush and Clifton¹³ had described an elevation of the proteolytic titer and a sharp and progressive fall in the antiproteolytic activity in dogs dying of pancreatitis incited by bile. In contrast, treatment with a soybean antitryptic factor had maintained the tryptic and antitryptic titers at normal levels in 3 dogs. Although these animals ultimately died, the investigators believed that 2 of the animals exhibited significant but transient improvement during the period of treatment. The tryptic and antitryptic titers in the present study failed to follow the patterns described by these authors to any consistent degree. The majority of animals, whether they survived or died, demonstrated an initial rise in the tryptic activity and a fall in the antitryptic activity after 2 to 4 hours.

SUMMARY

The necessity of an objective evaluation of infection in experiments on acute pancreatitis in the dog has been emphasized.

Whole blood therapy was far more effective than dextran in improving the survival rate in sterile trypsin-induced pancreatitis.

The failure of dextran stemmed in large part from its loss into the peritoneal cavity in the presence of increased capillary permeability.

A soybean antitryptic substance was ineffective in the therapy of experimental acute pancreatitis.

The antithrombin activity of the serum was not a reliable laboratory aid in experimental pancreatitis.

Serial determinations of the antitryptic and tryptic activities of the serum were not of prognostic value in experimental pancreatitis.

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A TECHNIC FOR RADICAL MASTECTOMY

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The general subject of breast cancer has been intensively cultivated recently. One group has attempted to sharpen our preoperative prognostic acuity to avoid useless operations; another has struck out in new directions to remove more cancer bearing tissues; physiologists and chemists are peering from their laboratories and suggesting hormones and cyclic steroids to slow abnormal growth. Our colleagues are removing powerful glands from cryptic and remote locations to knock the under-pinnings from cancer cells metabolism. Some are investigating little surgery and much x-ray as treatment, with a new concept—sheer survival—as a criterion of success.

Many moderately inarticulate, working surgeons still consider a radical mastectomy as a sheet anchor for treatment of carcinoma of the breast. They believe that the proper manual maneuvers are essential. This discussion will present, principally for resident consumption, a personal technic of radical mastectomy arrived at largely by adaptation of observed operations. (Details will be given with the hope that they will be found useful in the operating room.) The underlying philosophy of the operation is an attempt to remove the primary cancer and all of its lymphatic drainage channels in toto while cutting across only one of them.

A brief review of the anatomy will clarify this idea. The breast is in the medial portion of the anterior wall of the axilla. The subareolar lymphatics are actually in the skin overlying the breast. The skin incision must therefore remove all of the skin over the breast in order not to enter this lymphatic field. The lymphatic drainage of the breast ordinarily goes into the axilla and into the internal mammary chain. Breast cancer drains to other areas only exceptionally, and late in the history of the disease. By removing the skin over the breast, the pectoralis major and minor muscles, and the axillary contents, in one package, a radical mastectomy can be done without cutting any centrifugal lymphatic channels except those perforating with the internal mammary vessels into the mediastinum.

Considered generally, the axilla has 4 walls; a base and an apex (see figures 2 and 3). The base is the rounded skin of the axilla and a proper dissection is within 3 millimeters of this skin. The posterior wall is formed by the latissimus dorsi, subscapularis, and teres major muscles. The fascia over these muscles is removed. The anterior wall is formed by the pectoralis major, which is of course, removed in toto. The lateral wall is formed by the arm muscles and the medial by the rib cage, and intercostal muscles, all of which structures should be dissected clean.

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In reference to the entering and departing lymphatic channels, this package is pierced by the axillary nerves and vessels in the superior portion. The lymphatics of the arm drain into the mass; those of the neck do not ordinarily enter into it. Hence, an incision which severs the lymphatics from the arm does not cut vessels draining malignant tissue. An incision along the plane between the cervical and axillary lymphatics does not cut a lymphatic vessel. The long thoracic nerve and thoracodorsal run through the package vertically. The intercostal brachial nerve also pierces it. These structures are cut before they enter and after they leave the package, and thus the dissection in the V between the scapula and the thoracic cage is done cleanly without crossing lymphatic channels.

Removal of these three nerves mentioned produced no excessive deformity nor disability. In fact, the patients never bring up any complaints referable to their loss. Sectioning of the intercostal brachial nerve produces temporary anesthesia of the under arm. Removal of the long thoracic nerve is never noticed. The winged scapula (fig. 4), resulting from destruction of the thoracodorsal nerve can

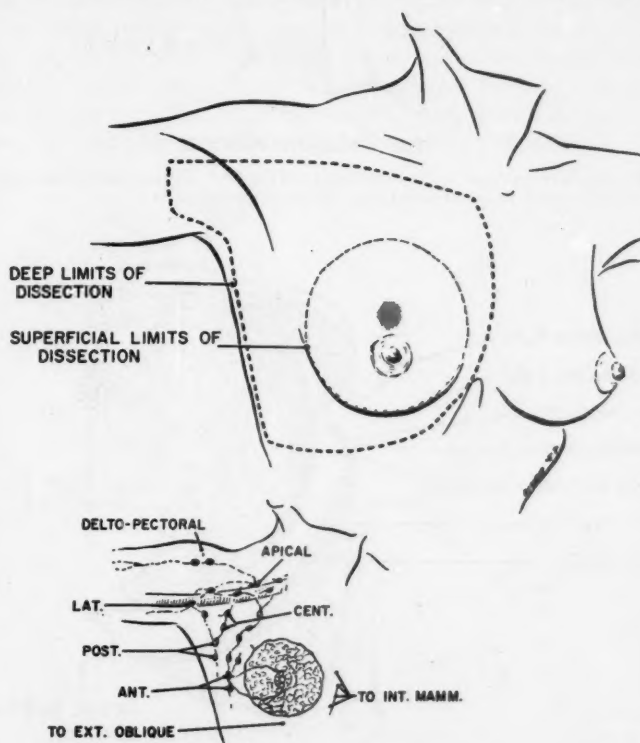
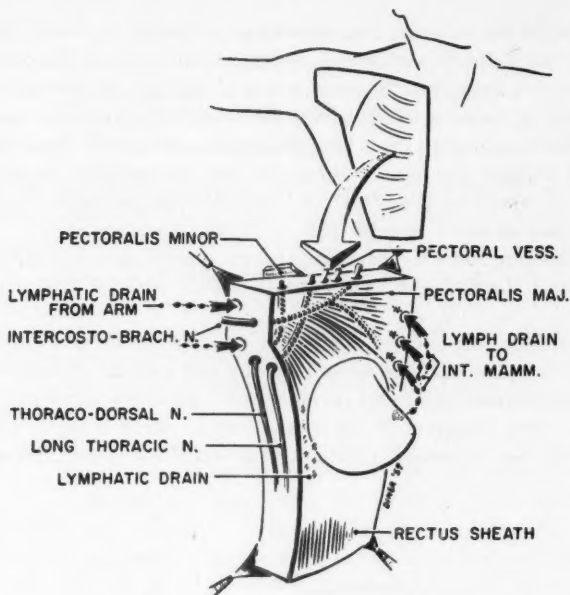


FIG. 1. A radical mastectomy is a good cancer operation. The primary lesion and its lymphatic spread (except the internal mammary) can be removed en bloc.



THE AXILLARY PACKAGE

FIG. 2. The axillary package to be removed showing that all lymphatic channels are removed en bloc except those draining into the mediastinum.

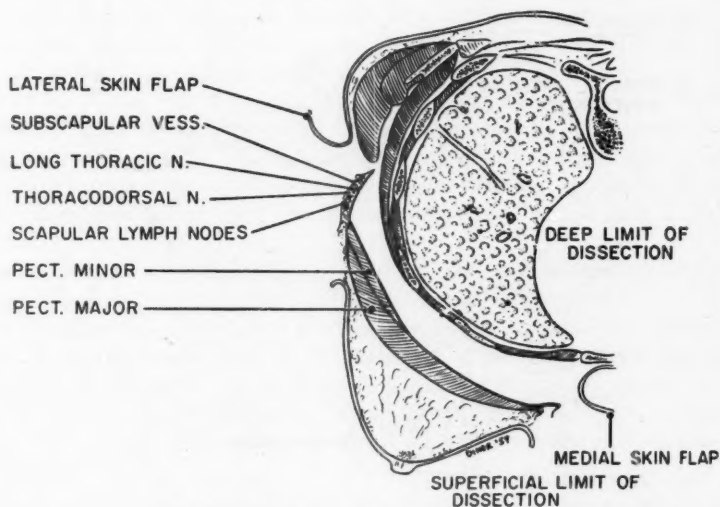


FIG. 3. Transverse section of axillary package

easily be seen but there is no disability and it is never mentioned by the patient or her family.

It is true that the internal mammary vessels leave the package medially and enter into another node relay station in the mediastinum. Perhaps an internal mammary gland dissection should be part of a radical mastectomy in medially placed lesions. The series now being run in Dahl-Iverson's Clinic will help to answer this question.

Now as to the care of the individual patient; once a suspicious lesion is seen, and by that I mean a single lump in the breast, the patient should be admitted to the hospital for surgery.

In some cases, aspiration of cysts can allow the seasoned clinician "to get away" without operation in selected cases. These cysts feel like a freely movable, greased marble. Even one familiar with these lesions must rigidly follow certain rules to avoid disaster. If the mass does not completely disappear with removal of the fluid; if the aspiration reveals blood in the cyst, or if the mass should recur in the same area, local removal is indicated. To violate these rules may result in unnecessary delay of treatment.

For the usual patient being considered preoperatively as a candidate for surgery, the criteria of operability for carcinoma of the breast proposed by Haagensen and Stout are now universally accepted; however, one must make judicious exceptions in the individual case. In patients with an early lesion, no roentgenograms are taken, but usually a chest film suffices in the search for



FIG. 4. Postoperative winged scapula from removal of long thoracic nerve: patient is unaware of any disability and has no complaint.

bony metastasis. In the more advanced lesions and particularly in the younger age group, intensive search by means of a skeletal series and chest film is in order. There are no general or medical contraindications to operation for cancer, but the patient should be brought into the best possible preoperative condition. This is ordinarily accomplished by cooperation with an internist, or the family physician. The physician anesthetist sees the patient the evening before surgery.

In the hospital, the patient is prepared for surgery by shaving the appropriate chest wall, axilla, and if a skin graft is anticipated, the entire abdomen. One pint of compatible blood is made available. The usual sedation of a barbiturate the night before and the morning of operation, with morphine and atropine an hour before surgery, is given. The patient is anaesthetized with Pentothal and maintained with nitrous oxide, until a definite decision as to the extent of the operation is made. As a cautery is used to control small bleeders, a nonexplosive anaesthetic mixture is used. The anaesthetist usually gives the patient 500 cc. of blood during the 4 hour procedure.

In the operating room, the ipsilateral arm is laid palm up, on an arm board, at right angles to the body and taped lightly in place across the hand. The head of the table is tilted up approximately 15 degrees. The appropriate half of the chest, entire abdomen, and the upper arm, is washed thoroughly with sepiisol and no staining dye is used. The operative site is draped with towels and sheets so that the abdomen may later be disclosed, and a graft taken from this area if needed. Donor sites on the abdomen usually heal better, and with less discomfort than those on the leg. The choice of site however, is a personal detail which may be discussed with the patient. It is best to avoid donor sites which ordinarily are subject to bands of clothing such as the brassiere or girdle.

With the patient in the operating room properly draped and prepared, the question is, to take a specimen for biopsy or not to. If one is sure of the diagnosis of operable carcinoma of the breast, no biopsy is taken. If reasonable doubt exists, however, a biopsy is obtained. When the lesion is small, it is completely excised, cut in the operating room, and a frozen section done. Excision is much preferable to incision. However, if the lesion is large, a small sliver of typical tissue is removed and a frozen section immediately made by the pathologist.

If the carcinoma involves the skin, fear of contaminating the area urges that no sliver be removed for biopsy, but that a complete excision be done. In some advanced medially placed lesions, the matter is discussed with the patient before operation, and a specimen for biopsy is taken from the second and third intercostal mediastinal node area. When this is done, the material is sent for fixed section, and the radical mastectomy done or not done, as a second procedure on another day. This is done because it takes an hour and a half to 2 hours to complete the biopsy of the specimen taken from the mediastinal nodes, and because these nodes are so small that fixed sections are necessary to demonstrate involvement or freedom from cancer. Therefore, it is necessary to do the procedure on separate days. At this time, if the mediastinal lymph nodes are found to be positive, radical mastectomy is not recommended.

After the usual biopsy, the instruments, gloves, and drapes are completely

changed; the wound having been packed with a sponge and closed with a running silk suture.

An incision is now made related both to the breast and to the tumor, but never into the true axilla itself (fig. 5).

A skin incision is begun a fingerbreadth below the midpoint of the clavicle and extended down to the skin over the breast. The skin over the breast itself is completely encircled. It is necessary to remove all of the skin over the breast tissue because the lymphatics of this area interconnect freely, and to leave this lymphatic field partially removed invites local recurrences. Extension of this incision in any direction is made to give the tumor 2 fingerbreadths margin. A vertical incision is carried down from the middle of the lower portion of the encircling incision 2 fingerbreadths down over the anterior rectus sheath. This incision is carried 2 to 4 millimeters deep into the skin (fig. 6). In the rare case where a lesion is placed far laterally into the axilla, a dart can be made in this area, or a skin flap can be moved upward from the skin over the latissimus dorsi, and the defect split grafted. The cardinal point, however, is that viable skin with adequate blood supply must be used to cover adequately the true axilla in complete abduction. Any size defect on the chest wall can be readily covered with split thickness grafts without loss of function. Such coverage will allow normal function of the arm and promotes good healing. It is my belief that postoperative edema is the result of delayed healing, or of recurrence of the tumor.

The next step is to raise the lateral skin flap from the rectus sheath to the white tendon of the latissimus dorsi muscle, to expose the lateral wall of the axilla, and

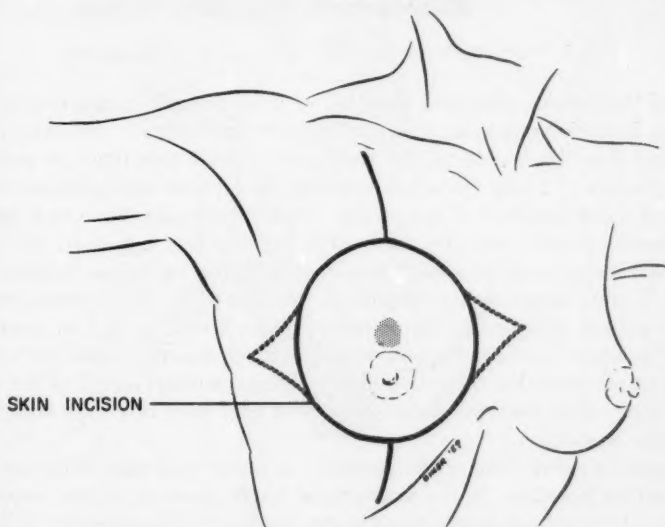


FIG. 5. Skin incision

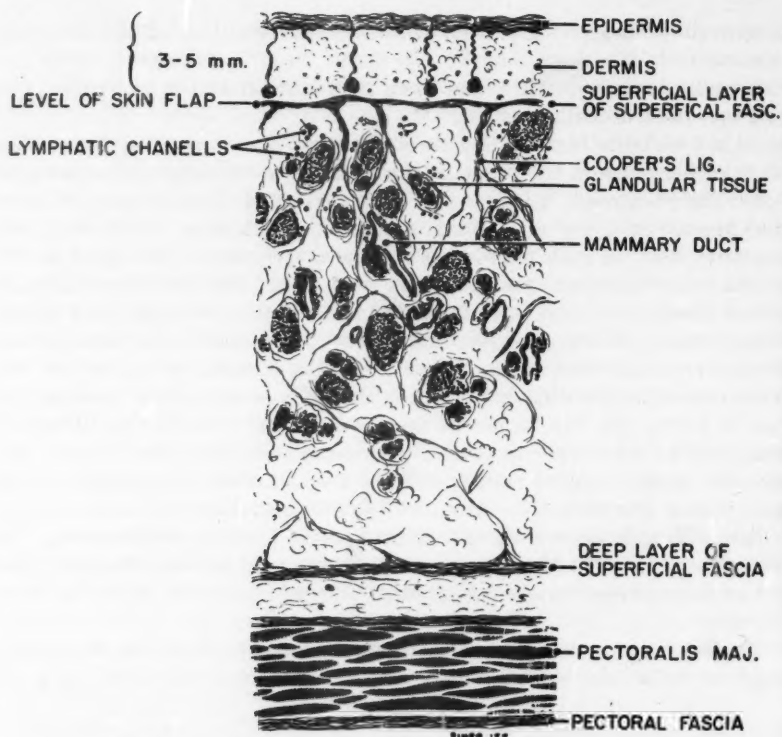


FIG. 6. Transverse section of skin to show level of dissection

to unroof the curving edge and insertion of the pectoralis major muscle. This dissection is carried out at an even depth below the surface of the skin; raising flaps about 3 millimeters thick (figures 6 and 7). Such thin flaps are necessary because strands of breast tissue often extend close to the skin especially in the upper and outer quadrant of the breast. Thicker flaps may leave such parts of the mammary gland in situ. In starting the flap, the skin is grasped with heavy forceps and about a cm. of dissection is done from the top to the bottom of the incision. Towel clamps are now placed on the skin edges. The operator holds 2 of them, pulling straight up. The assistant places a wet lap pad on the breast, and gently makes counter traction with one hand; catching bleeders with the other. A small amount of dissection is done along the entire length of the wound at each time. Then the hemostats are touched near their tips with cautery and the process repeated.

The superior lateral limit of this dissection is the arching mass of the pectoralis major and its insertion. In the inferior and lateral portions of the wound, the dissection is carried out laterally to $1\frac{1}{2}$ cm. beyond the border of the latissimus dorsi. Inferiorly, it is carried down 2 fingerbreadths over the anterior rectus

sheath, but the anterior rectus sheath is not entered. The latissimus dorsi may be difficult to locate in poorly muscled, obese patients. It can be found by demonstrating the rectus sheath on the abdominal wall, then cutting down vertically to the chest wall; extending this incision laterally at the lower end of the incision until a muscle running vertically is found. This must be the latissimus dorsi, and it will mark definitely one limit of the dissection. Dissection can then be carried upward freeing the lateral border of the latissimus from subcutaneous tissue. This "red line of Shemke" marks the lateral limit of the block incision of tissues. After the latissimus has been well demonstrated all along the chest, dissection is carried medially between the latissimus and the serratus anticus muscles in the groove between the latissimus and the chest wall freeing it for a distance of about 1 cm. As the dissection is carried from below upward about 2 to 2½ cm. of the white tendon of the latissimus dorsi is exposed. This area is now close to that of the axillary vein, so dissection at this point is transferred to the superiomedial area (unless one wished to make careful search for the axillary vein in the lower axilla). If dissection is carried too far medially and posteriorly in the axilla, one runs into the subscapular veins, and the artery and veins thoracolateralis.

To return to the dissection of the superior end of the lateral skin flap. The insertion and lower edge of the pectoralis major can now be clearly palpated if

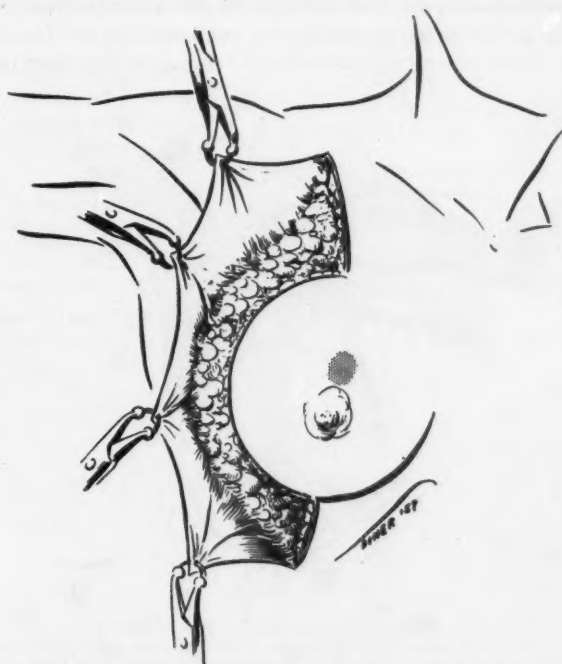


FIG. 7. A thin lateral flap is developed first

not seen. The skin flap underlying the superior vertical incision is now raised as high as the costoclavicular junction superiorly, and to the midline medially. It is carried laterally about on a line with this to the insertion of the pectoralis major. This insertion of the pectoralis major muscle and the lateral edge of the latissimus dorsi muscle outlines the lateral edge of the block to be removed. This is the location of the so called "red line of Shemke".

To define the superior limit of the package, a perpendicular transverse incision is made through the fat at the limits of the upper portion of the wound down to the fibers of the pectoralis major. The tissue overlying the pectoralis is put under tension by sponge in the left hand and pulled caudad. Using the knife, all of this is cleaned off the pectoralis major down to the division between the clavicular and sternal heads (fig. 8). Two small arteries will usually be cut. One can now see the split between the sternal and clavicular heads of the pectoralis major. This split does not extend vertically through the muscle, but runs from the surface of the muscle superiorly towards the deeper portion at about a 45 degree angle. It is entered into at the midpoint of the clavicle with the back of a Bard-Parker knife until the costoclavicular or deep pectoral fascia is felt. The knife blade is carried medially and laterally to the ends of the muscles. The index finger of the appropriate hand is put into the split and the second assistant retracts the skin over the humerus with a medium sized Richardson retractor. The finger can now be passed at the level of the humeral head laterally and caudadly over the humerus encircling the pectoralis major. Occasionally the insertion can be cut without putting a finger beneath it. The insertion is severed



FIG. 8. The lateral and upper skin flaps have been turned back. The pectoralis major is split between the clavicular and pectoral heads because the cervical lymphatic system stops here and does not interconnect through the muscle with the lymphatics of the breast.

with a scalpel close to the bone. The proximal stump is seized in a Kocher clamp for future retraction. There usually is a small bleeder in the stump of the insertion, but it is easily cauterized. This maneuver nearly always exposes a slip of the pectoralis major arising from the lower ribs which has a separate tendon of insertion into the humerus. These tendon strands are cut with a knife and the pectoralis major freed from the fascia overlying the brachial artery and vein, and down towards the chest wall. This exposes the coracoclavicular fascia.

Sometimes one sees muscle tissue arching over the artery and vein obscuring the fascia. These atypical muscles are numerous and may be slightly confusing. They consist of additional groups paralleling the pectoralis major muscle or running from the latissimus dorsi to the humerus. They are summarily removed at this stage, and the lateral axilla thus exposed. We have now finished the dissection of the base and part of the lateral wall of the axilla.

One now proceeds with the dissection of the rest of the lateral wall of the axilla composed of the fascia around the axillary vein and brachial plexus, and that over the subscapular muscles. At the same time, the superior limit of dissection is defined. The exposed fascia overlying the axilla, artery, vein, and plexus may be safely entered into swiftly, by pulling downwards on it with a sponge and cutting transversely along the lower border of the coracobrachialis (fig. 9). If this is done on the humerus, it is without danger. It loosens the axillary fascia and allows cautious definition of the lateral end of the axillary dissection

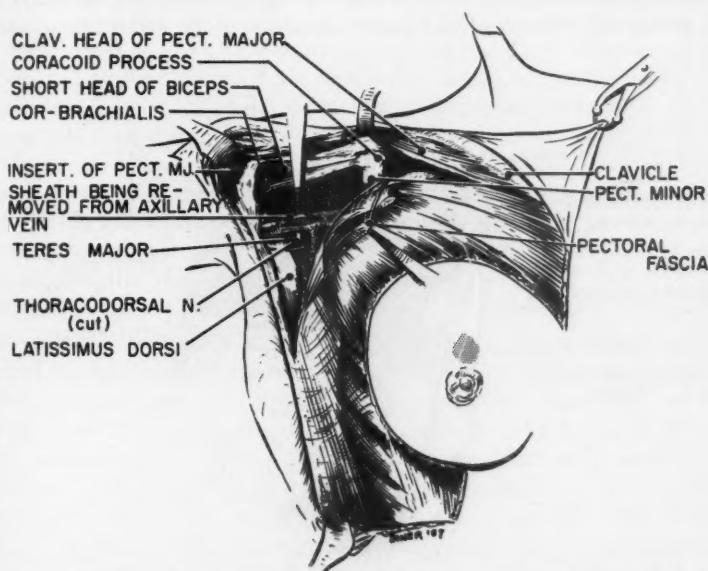


FIG. 9. The insertion of the pectoralis major having been removed from the humerus; the brachial lymphatics flowing centripetally are cut across and carried medially with the sheath of the vein. The coracobrachialis and pectoralis minor muscles are exposed. The lymphatic sheath over the latissimus dorsi muscle is cut. The axillary contents are visible and the long thoracic nerve is cut to avoid entering the axillary package.

by making longitudinal incisions over the vein and plexus. These tissues are clearly defined and this tissue is drawn medially taking with it the sheath of the vein. One can be sure of getting the sheath of the vein by watching the vein expand when the sheath is removed. Dissection is carried medially along the brachial plexus until the axillary artery is exposed. This can be used as a mark for the upper limit of the dissection here, but there is occasionally a small amount of tissue on the humeral head where the coracobrachialis inserts which is nice to clean out. Smaller vessels, the thoracoacromial, which are nutrient to the pectoralis major are now encountered. They are clamped and cauterized as one comes to them. However, any vessel arising close to the main artery or its vein is tied. The coracoclavicular membrane is removed as we move medially and the lateral edge of the pectoralis minor is exposed (fig. 9).

To expose the medial third of the upper end of the dissection, one must remove the pectoralis minor. The medial edge of this muscle can be demonstrated with blunt dissection and a finger is slipped around the pectoralis minor tendon high up in the neck towards the scapula (fig. 10). This finger is run down to the scapula and the insertion of the pectoralis minor cut at the scapula. There will usually be a 2 or 3 millimeter arterial bleeder in the stump, which is now caught, and cauterized. Occasionally it is necessary to pack this area with a sponge temporarily. A Kocher clamp is placed on the edge of the pectoralis minor and it is gently pulled caudad for tension. Using Metzenbaum scissors, all the tissue over the axillary artery and vein is removed, again continuing to include the sheath of the vein. The nutrient vessels and nerves of the pectoralis major and

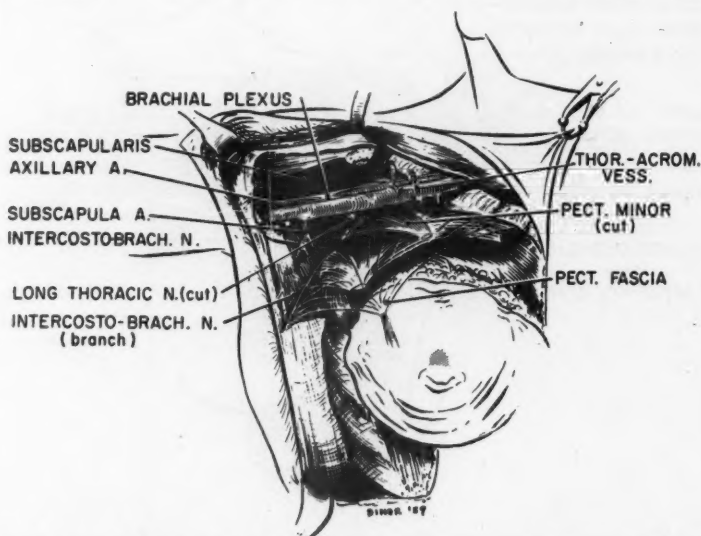


FIG. 10. The teres major and subscapular muscles are exposed. The nutrient vessels to the pectoral muscles are tied. The thoracodorsal nerve is cut. The pectoralis minor is removed from its insertion and dissection carried medially.

minor are separately dissected out, clamped, cut and tied. This should result in completely freeing the superior surface of the axillary vein down to the coracoclavicular ligament, and completes the upper limit of our package.

To finish the lateral dissection of the lateral axillary wall and to get to the posterior wall, it is now sometimes convenient to begin the dissection again laterally at the skin of the axilla using the pectoralis major for tension and pulling it medially. This allows dissection around the lower portion of the vein down along the lateral border of the axillary skin to free the remaining portion of the white tendon of the latissimus dorsi, which was not cleared before (fig. 7).

Dissection is now carried out in three planes alternately. The lateral skin flap is put on tension, and dissection is continued down inside the latissimus dorsi muscle on top of the subscapular muscles. In this area, one encounters the two motor nerves and their accompanying vessels. These are cut and tied. One also finds in the superior portion of this plane, the subscapular vein, which is dissected free and allowed to remain intact as it soon passes posteriorly. After the lateral dissection has been carried to the chest wall, the next step is to demonstrate the posterior superior surface of the medial end of the axillary package and to dissect in this plane until one joins the lateral plane. The medial skin flap is pulled medially on tension, and with the back of the scalpel, one enters into the tissue plane, lying beneath the pectoralis major on top of the intercostal muscles. This dissection is carried along the edge of the ribs towards the bottom of the V in the angle between the ribs and the scapula. Dissection is also carried along the superior margin of the package. In this area, the two motor nerves and their accompanying vessels are again found and cut. One continues this dissection until the chest wall, the area below the axillary artery and vein, and the subscapular area have been cleaned out. The portion between the latissimus dorsi and the serrati are cleaned out further, if this is not done adequately before. The dissection from superiorly is carried down to about the third or fourth rib where it meets the dissection plane coming from medially. The dissection from the lateral side is carried up to clear the inter-digitations of the serrati all the way from the rectus sheath to the top of the axilla (fig. 11). Hot, wet sponges are now placed in the area.

The next step is to define the medial line of dissection and to remove the origin of the pectoralis major there. The medial skin flap is raised to the midline, and inferiorly as far as the rectus sheath. When the skin is retracted medially, the fat is incised down to the midline of the sternum to mark the "red line of Shemke" here. A finger is now placed from above downward beneath the origin of the pectoralis major. With a little tension to put the muscle on stretch, the pectoralis major is severed from the chest wall, clamping the perforating internal mammary vessels as they are demonstrated. These are now controlled with cautery, and the specimen allowed to drop laterally. We now finish removing the posterior wall of the axilla. The pectoralis minor is shaved off the intercostal muscles (fig. 10). This can rapidly be removed in the superior portion because there is very little blood supply. In the inferior portion, however, there are con-

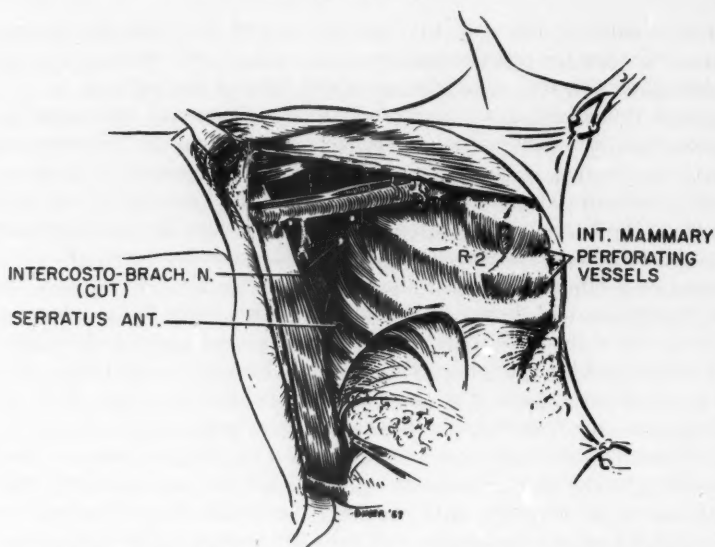


FIG. 11. The pectoral muscles are removed from the chest wall. The perforating branches of the internal mammary lymphatics are tied. Here and only here centripetal lymphatic spread is transected.

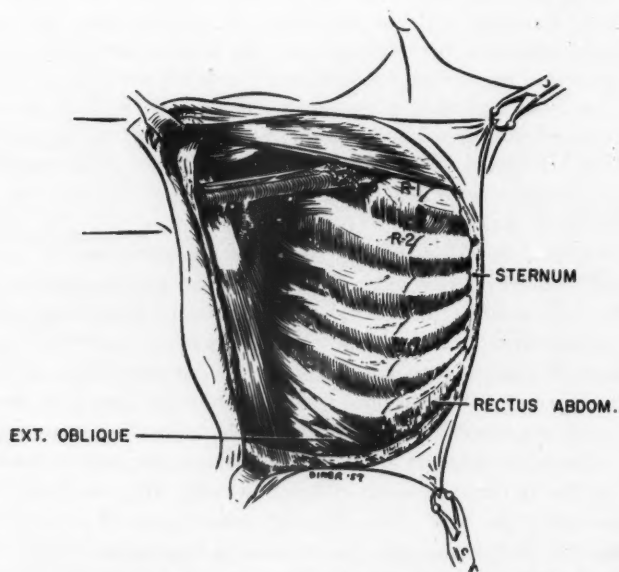


FIG. 12. The axillary package completely removed

siderable vessels coming through from the chest wall, and they have to be picked up at this scene.

This completes the dissection of the breast and axillary package; removing in toto all of the axillary lymph node drainage, but cutting across lymphatic channels draining from the breast into the mediastinum (fig. 12). It may be that the internal mammary nodes should be removed in the same setting.

The tissue being removed, one turns to the restoration of function. The wound is flushed out with normal saline solution and inspected for bleeders and sponges which may be tucked away here and there. The skin flaps are sewn to the chest wall without tension. Special care is taken to assure a very full covering of the depression in the axilla below the artery and vein. Actually, one ordinarily sews the upper skin flap to the second and third rib. Doing this will insure mobility of the arm, proper healing, and prevent postoperative edema (fig. 13). A sump pump is inserted over the tenth rib in the posterior axillary line, to drain the lateral skin flap. No drain is placed under the medial flap. No drain is placed in the upper axilla, but a small catheter may be inserted and brought out on the chest wall through an incision which is not in the axillary area. If a drain is brought out in the axillary area, any induration or failure of wound healing in the drain site will help to bind down the arm, and prevent complete abduction. This small catheter is best fashioned as a sump pump with a T tube in one side of which a small polyethylene tube leads down almost to the end of the catheter. The other end of the T tube will now be placed on suction

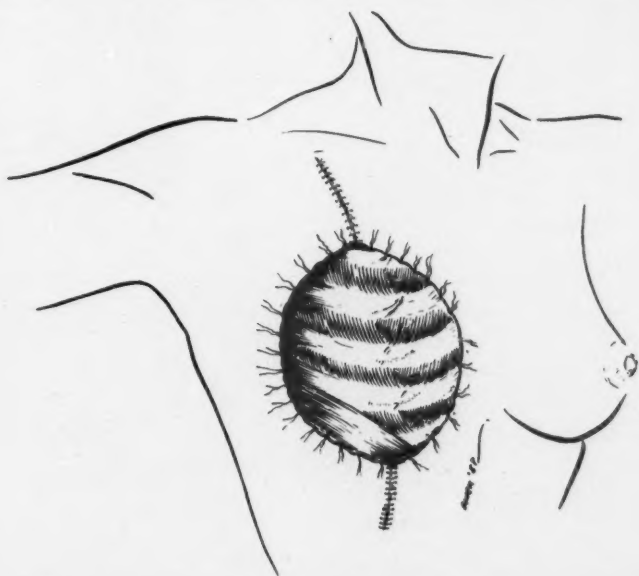


FIG. 13. The skin flaps are loosely tacked to chest wall with ample skin in the axilla for abduction.

for 24 hours. A split graft is now cut from the abdomen with the electrodermatome and sewed in place on the chest wall. A sterile greased gauze is placed over it, and then 4 by 4 sponges taped down. Mechanics waste is packed into the axilla. Pressure is applied to all flaps usually with elastoplast dressing held in place with 2 inch adhesive tape along its margin (fig. 14). This is applied by spraying the skin with canned tincture of Benzoin, putting on a piece of elastoplast, then applying a piece of 2 inch adhesive tape along one margin, then another elastoplast with more tape, until the dressing is completed alternately. Excellent pressure may be obtained by using 3 inch Ace bandages.

To care for the donor site, a piece of dry, sterile linen is placed on it. On top of this is immediately placed a 4 by 4 sponge saturated with hot saline solution. As soon as the dressing of the primary wound is completed, the 4 by 4's over the donor site and over the linen are removed. The patient is sent to the recovery room with nothing but sterile linen over the donor site. This will soon dry. If it be kept dry, it will become and stay sterile, and function as an eschar. If adhesive tape is placed across it, the area underneath the adhesive tape will become moist and therefore not sterile. The whole point of this dressing is to keep it dry. It will cause no discomfort and can be taken off in about 10 days. It relieves the patient the necessity of bulky donor dressings, the possibility of infection, and of course, cuts down on the expense to the hospital.

As to the unique postoperative care of these patients, the sump pump catheter is brought out in 24 hours, the breast incision is dressed on the third day, and

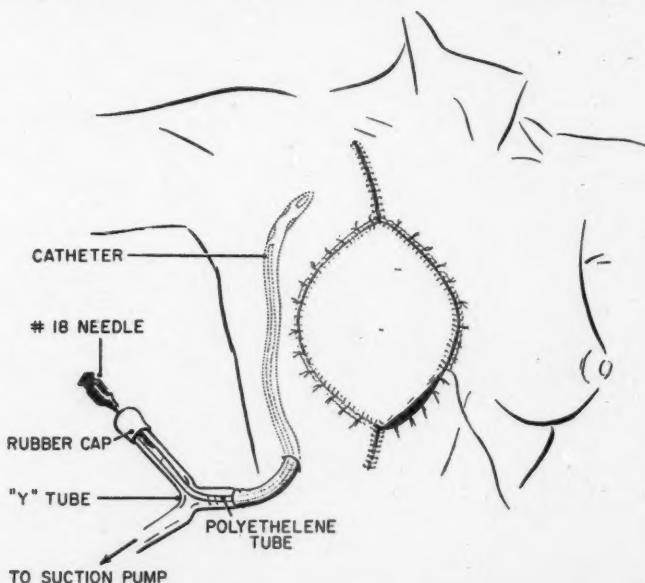


FIG. 14. The defect is covered with a split thickness graft and the flaps drained with suction or Penrose drains.

part of the stitches, holding the graft in place, are removed. The tissue drain is withdrawn at the same time, and any serum collections which are found are aspirated. The wound is dressed again on the fifth day, and the remaining stitches removed. The patient is encouraged to move her arm freely as soon as she will and it is raised over her head on the third day when the wound is dressed. If a serum collection of over 25 cc. persist on the fifth day, the drainage should probably be reinserted. No antibiotics are given. The patients do not ordinarily require transfusions. They can expect to go home from the hospital on about the tenth day for further follow up care by their surgeon or the family physician.

This operation so done will result in the local cure of carcinoma of the breast.

INTESTINAL OBSTRUCTION DUE TO FOOD BOLUS FOLLOWING GASTRECTOMY*

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The occurrence of small bowel obstruction due to food bolus has been reported many times. However, little emphasis has been given to obstruction following gastrectomy when lowered gastric acidity, a larger opening from the stomach and more rapid emptying of the stomach make this event more likely. Siefert⁷ reported the first such case in 1930 when sauerkraut formed the obstructing bolus. Norberg⁶ has recently reported 7 cases following subtotal gastrectomy with 4 of these due to orange slices. Allen and Smithwick,¹ Bowen,³ Baumeister and Darling,² Fleming and Ward-McQuaid,⁵ Spurzem and Desser,⁸ and Elfving and Scheinin⁴ have reported similar cases.

We have operated upon 2 patients within a 3 month period with obstruction from orange slices following gastrectomy. In both cases, the patient was edentulous and was not wearing dentures while eating oranges.

CASE REPORTS

Case 1. R. C. M., a 61 year old white veteran, was admitted to the hospital on Jan. 18, 1956, with a complaint of intermittent right upper quadrant cramping pain. He had a subtotal gastrectomy and vagotomy performed in 1947. Subsequently, he had two laparotomies for small bowel obstruction due to adhesions. The physical examination on admission did not reveal any evidence of small bowel obstruction, and the patient was started on a diet. An upper gastrointestinal x-ray series and small bowel series showed a normal functioning gastrojejunostomy without evidence of obstruction in the small bowel. The patient has been edentulous since 1946 and did not wear dentures. He was progressing satisfactorily on a 5-meal bland diet until Jan. 30, 1956, approximately 12 days after admission. At this time, he complained of upper abdominal pain, intermittent in character. The physical examination revealed minimal signs of obstruction with hyperperistalsis. A Kaslow tube was inserted with continuous suction and intravenous fluid therapy administered. Within 6 hours the distention and pain had increased so that abdominal exploration was indicated. Under endotracheal anesthesia, the abdomen was explored through a right paramedian incision. Two masses were found in the ileum about 20 centimeters and 15 centimeters from the ileocecal valve which were completely obstructing the ileum and pitted on fingertip pressure. The ileum was opened longitudinally and the masses consisting of several packed orange sections were removed from the lumen of the bowel (figs. 1 & 2). The opening in the bowel was closed transversely with an inner layer of catgut and an outer layer of interrupted silk suture. His postoperative convalescence was uneventful. Further questioning of the patient revealed he had eaten an orange about 10 p.m. on Jan. 25, 1956. Pathologic Specimen: The major specimen consists of 6 slices of orange which have not been masticated. The smaller specimen consists of 2 slices of orange slices which are also intact. Both are bound together loosely but can be readily separated (figs. 1 & 2).

Case 2. E. V. C., a 36 year old white male veteran, entered the hospital at 5 a.m. March 17, 1956, with a complaint of cramping abdominal pain without vomiting of 15 hours' dura-

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FIG. 1. The two undivided boluses of orange slices found in Case #1



FIG. 2. The large bolus of food after being separated showing it to consist of six separate slices.

tion. In June 1953, a subtotal gastrectomy had been performed for a bleeding duodenal ulcer, subsequent to which the patient was in excellent health. The physical examination on admission revealed moderate abdominal distention with tinkling bowel sounds, occasional peristaltic rushes, and generalized mild abdominal tenderness. An intestinal tube was passed and continuous suction maintained. Intravenous fluid therapy was initiated. He obtained little relief from this therapy, and 12 hours after admission an exploratory laparotomy was indicated. Under endotracheal anesthesia, a right paramedian incision was made and dilated small bowel was present to within 12 centimeters of the ileocecal valve, where a mass was found obstructing the lumen. The mass pitted on pressure but could not be moved by manipulation. The ileum was opened longitudinally and a bolus of orange slices removed

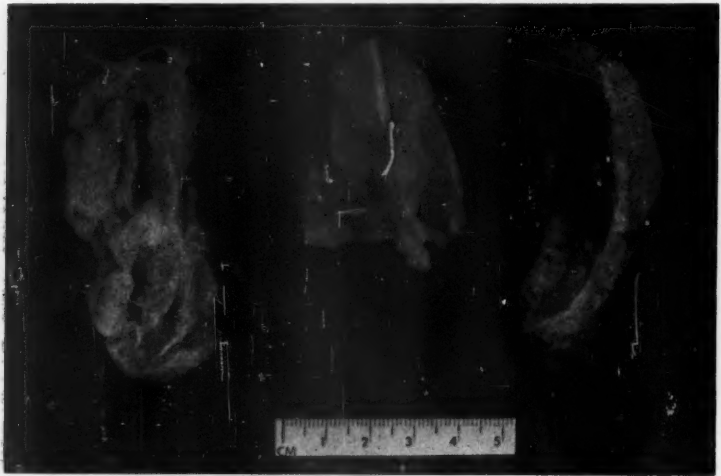


FIG. 3. The three orange slices which formed the obstructing bolus are shown after separation (case #2).

from the lumen (fig. 3). A transverse closure was performed using catgut for the inner layer and interrupted silk sutures for the seromuscular layer. He had an uneventful course with oral feeding being resumed on the third postoperative day.

Pathologic Specimen: Pathologic examination reveals 3 large segments of orange, the largest measuring 7 by 3 by 2 centimeters. Grossly they are almost intact segments, and show relatively little effect of digestion. On microscopic examination there is evidence of considerable digestion (fig. 3).

DISCUSSION

The rapid emptying of the stomach following gastrectomy is a well known fact, allowing less time for digestion by the gastric secretions. The lowered acidity subsequent to the gastrectomy would seem to be an additional factor. The usual gastrojejunostomy will also allow a larger bolus of food to pass than would a normal pylorus.

Both of the patients presented do not wear dentures, which undoubtedly increases the chances of an obstruction due to swallowing larger boluses of food.

Both cases presented had obstruction due to orange slices; but any bulky food, especially citrus fruits, could be a cause.

The appearance at the operating table is important. A small bowel tumor may be suspected at first; but the bolus pits with pressure and can usually be moved on gentle manipulation. The bowel at this site appears to be normal. On occasions, the bolus may be manipulated through the ileocecal valve.

SUMMARY

Two cases of orange slice obstruction following gastrectomy are presented. The lowered gastric acidity, large opening from the stomach, and more rapid

emptying of the stomach following gastrectomy makes such an event more likely.

All patients having gastrectomy should be cautioned not to consume bulky foods, especially large pieces of fruit pulps, which may form a bolus and cause subsequent intestinal obstruction.

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VESICoureTERAL REFLUX IN CHILDREN

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The subject of vesicoureteral reflux has been one of intense speculation for many years with conflicting opinions as to whether it occurs in a normal child.

Although the idea of a valvular mechanism has been more or less discarded, there is still no one accepted explanation of why urine from the bladder does not regurgitate up the ureters into the kidneys. Most investigators are satisfied to accept the oblique course of the ureter through the wall of the bladder as sufficient explanation, intravesical pressure causing compression of the intramural portion of the ureter.²

The mechanism of vesicoureteral reflux in obstruction is best stated in the words of Graves and Davidoff³ that "Reflux depends primarily on sustained tonus of the bladder musculature as it actively resists distention." This is noted clinically in a bladder which has hypertrophied to overcome an obstructed vesical outlet, as evidenced by a thickened detrusor and advanced trabeculation, even though the amount of residual urine is moderate. On the other hand, a tabetic patient with an atonic dilated bladder may carry enormous quantities of residual urine for years without suffering any ureteral dilatation as evidence of reflux.

More cases of ureteral reflux are being found since the ordinary cystogram has been discarded and special technics substituted. Reflux may be demonstrated with a voiding cystogram in which a film is exposed while the patient is straining to void, when it is not demonstrable with a routine cystogram. Also, Stewart⁴ and Bunge¹ have shown that reflux may be present in a delayed cystogram when not present in a film exposed immediately after the introduction of contrast medium into the bladder. Our experience with delayed cystography as compared with the voiding cystogram has revealed equally satisfactory demonstration of reflux in either one. Voiding cystography has the advantage of no waiting period and there are obvious handicaps in a small child with the delayed cystogram.

Excretory urograms are misleading as it is not uncommon to see serious vesicoureteral reflux in patients considered to have normal pyelograms.⁶ This should always be considered in those cases of persistent infection in which recurrence occurs in spite of normal appearing pyelograms (fig. 1 A, B).

There are obvious cases of vesicoureteral reflux in which the typical history and physical findings of bladder neck obstruction are obtained (fig. 2, A, B). These produce no problem of diagnosis but become difficult in management in those with far advanced renal deterioration. These are the patients with a long overlooked history of recurrent urinary tract infection. There may be a history

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FIG. 1A

FIG. 1B

FIG. 1. A. Intravenous pyelogram. B. Same case, cystogram

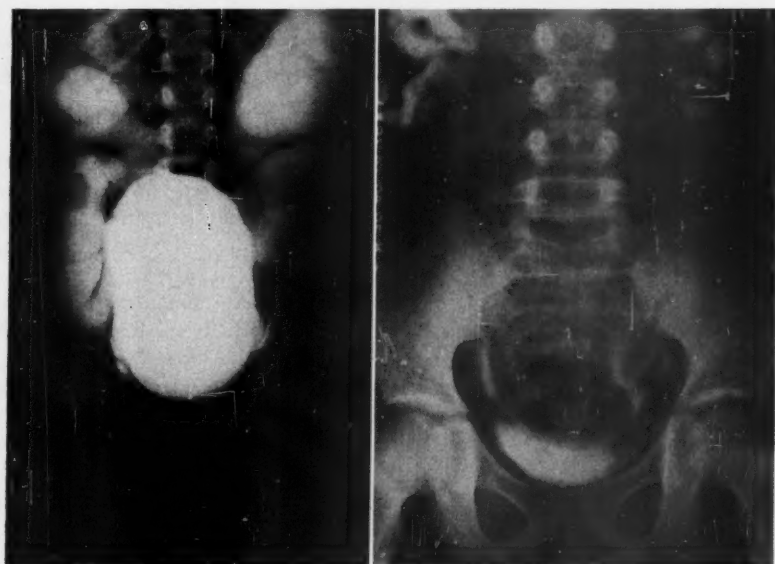


FIG. 2A

FIG. 2B

FIG. 2. A. Bladder neck contracture with reflux. B. One year later following transurethral resection, partial cystectomy and resection of redundant ureters.



FIG. 3A



FIG. 3B

FIG. 3. A. Intravenous pyelogram in case of recurrent infection. B. Same case, cystogram, (note reflux).

of frequency, intermittency, difficulty, hesitancy and enuresis. The over-distended bladder is sometimes palpable and as renal injury progresses, symptoms of uremia in its advancing stages appear.

On the other hand, some of the less advanced cases do not offer such definite suggestions of obstruction (fig. 3 A, B). These are the reversible cases with less obstructive symptoms and possible recurrent infection. Repeated meticulous study is required if symptoms persist. Some cases are not apparent on first examination but will be later on.

Our chief interest in this problem stemmed from those patients with minimal symptoms, such as an attack or so of infection, in which voiding cystography revealed vesicoureteral reflux. Cystoscopic examination of such patients may reveal very minimal trabeculation of the bladder wall and one is confronted with the decision of whether to recommend surgery on the vesical orifice.

There are divergent opinions in the literature regarding the question of whether ureteral reflux occurs in the normal patient.

In an effort to satisfy our own curiosity, an investigation was initiated with the desire to determine if reflux occurred in children without history or findings suggestive of urinary tract disease.

One hundred routine admissions, of both sexes, to the Pediatric Service were subjected to voiding cystography. These were patients who had a nonurological admission with a negative urinalysis. The examination was performed following the recovery from their disease when ready for discharge from the hospital. The

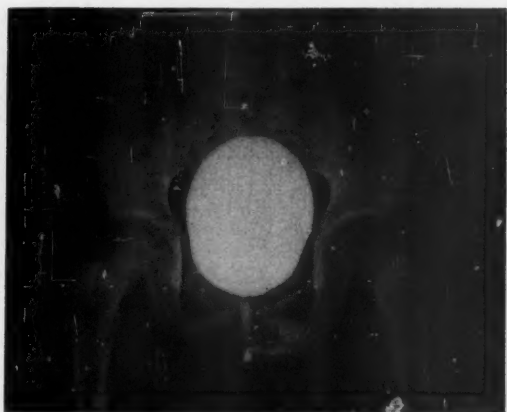


FIG. 4. Normal voiding cystogram

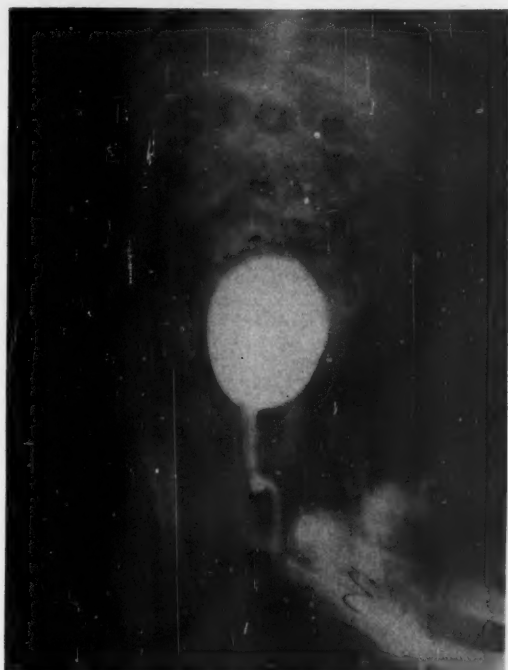


FIG. 5. Voiding cystogram with reflux

children ranged in age from 14 days to 14 years, averaging 3.5 years. The diagnoses were those usually seen in a general pediatric service.

No anesthesia, local or general, was used. Ten per cent sodium iodide was introduced through an appropriate-sized urethral catheter by gravity until the

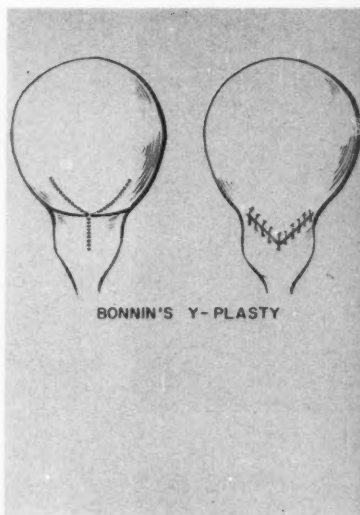


FIG. 6



FIG. 7A

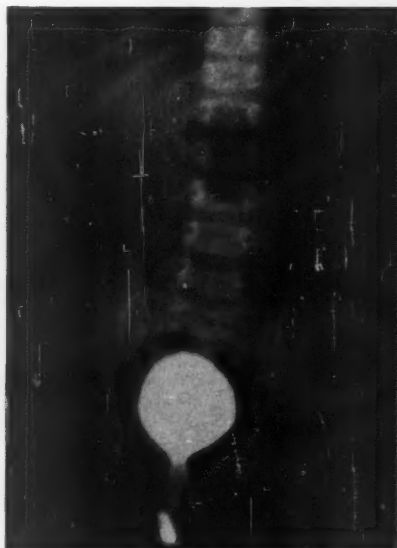


FIG. 7B

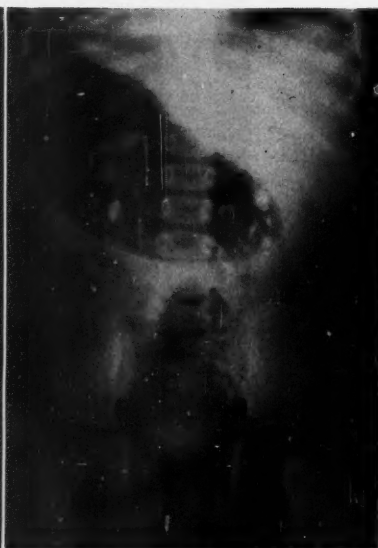


FIG. 7C

FIG. 6. Drawing, cystoplasty

FIG. 7. A. Intravenous pyelogram, bladder neck contracture with bladder calculus. B. Postoperative bladder neck Y plasty. C. Postoperative intravenous pyelogram.

flow stopped. Then by means of a bulb syringe, $\frac{1}{2}$ to 2 ounces, depending on the size of the patient, was instilled. A voiding cystogram was obtained with the patient in the supine position (fig. 4).

Of the 100 children examined, only 1 exhibited vesicoureteral reflux (fig. 5). None of these had fever or other evidence of urinary tract infection following examination.

The 1 patient exhibiting reflux was a 4 month old male admitted to the hospital for malnutrition. He had a negative urinalysis and a normal nonprotein nitrogen. Cystoscopy revealed a bladder neck contracture and moderate trabeculation of the bladder musculature. A transurethral resection of the bladder neck was performed with an uneventful postoperative course.

The surgical approach to this problem may be either transurethral or retropubic. We have been satisfied with the transurethral resection of the vesical orifice in spite of some of its technical difficulties. In general, this approach is used unless some other factor such as stone or diverticulum demands open bladder surgery. If so, the Bonnin Y plasty applied to the bladder neck is used⁴ (fig. 6). In some, the dome of the bladder is so atonic that even though the obstruction is relieved, there is still residual urine due to incomplete contraction of this area. In these a partial cystectomy is applied at the same time (fig. 7 A, B, C).

SUMMARY

All children with recurrent urinary tract infection demand complete urologic studies including voiding cystography.

Vesicoureteral reflux is indicative of uropathy and the normal urinary tract will not exhibit reflux.

The surgical approach for vesical neck obstruction may be either transurethral or retropubic. The decision depends on concomitant bladder pathology.

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EXPULSION OF SEQUESTERED ILEUM THROUGH A FECAL FISTULA

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Intussusception is unusual in adults. Sequestration of an intussusceptum with spontaneous expulsion and auto-anastomosis of the remaining bowel is rare. This report is the first instance of expulsion of the sequestered bowel through a fecal fistula.

Eighty-five per cent of all intussusceptions occur in children under 2 years of age. The cause of intussusception in this age group is seldom known. The cause in adults, however, is usually a mass in the lumen of the bowel or bowel wall, as shown by Danhauser⁴ in 668 collected cases. Eleven (11) previous cases of spontaneous expulsion with auto-anastomosis have been recorded in the American and English literature.^{1-3, 5-11}

CASE REPORT

A. B., a 45 year old white man entered a local hospital on May 20, 1953, with severe abdominal pain of sudden onset. Peptic ulcer symptoms had been present for 2 years preceding this episode. A diagnosis of perforated ulcer was made and a duodenal ulcer was closed 12 hours after admission. A stab wound drainage was done at McBurney's point on the fourth postoperative day because the patient was not responding to treatment for peritonitis. Three days following the drainage a fecal fistula developed through the stab wound. Abdominal distention and pain continued throughout his hospital stay, but oral feedings were continued. Spontaneous bowel movements occurred through the fecal fistula.

The patient was transferred to Veterans Administration Hospital approximately 6 weeks later on June 29, 1953. The physical examination on admission revealed the patient to have a temperature of 100.4F., pulse 92 per minute, and blood pressure 130/70 millimeters of mercury. The patient was markedly emaciated: movement of any type caused a great deal of abdominal pain. The abdomen was moderately distended, with a healed recent upper right rectus incision. A fecal fistula over McBurney's point was draining semiformal stool. A firm, tender, nonmovable mass extended from the pelvis to 2 centimeters below the umbilicus. The pelvic mass was firm and tender on rectal examination. On auscultation peristalsis was markedly diminished.

On admission the hemogram revealed 13,000 white blood cells per cubic millimeter, with 78 per cent neutrophils, sedimentation rate 51 millimeters, and hemoglobin of 12.5 grams. The fasting eosinophils was 22. The urinalysis and stool examinations were normal. Total proteins were 6.1 milligrams per cent with 3.4 milligrams per cent serum albumin. Blood chemistries throughout the hospital course were normal. Roentgen examination and fluoroscopy upon entry into the hospital revealed a negative chest, good diaphragmatic motion, minimal amount of small intestinal gas, a relative absence of gas in the pelvis, and evidence of an extraluminal pelvic mass. A fecal fistula in the ileum, 4 centimeters from the ileocecal valve, was demonstrated by barium enema. An upper gastrointestinal series showed some dilatation and retention of barium for more than 24 hours in the region of the terminal ileum.

The patient received blood transfusions, chemotherapy and mild sedation as initial treatment. The temperature spiked to 100 daily for the first 5 days, then became normal.

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Cul-de-sac aspiration under spinal anesthesia yielded a small amount of seropurulent material. Following this procedure, there was a decrease in size of the pelvic mass. Symptoms of partial small bowel obstruction continued, although the patient was taking oral feedings. Three feet of devitalized material was extracted through the fecal fistula on July 23, 1953, the material appearing to be bowel. The pathologic sections verified this impression. The patient then began having regular bowel movements by rectum and the fecal fistula almost completely closed. However, he continued to have recurrent partial small bowel obstruction, during which time the drainage through the fecal fistula increased.

On Sept. 29, 1953, the abdomen was explored through a low right transverse incision and several loops of edematous, hypertrophied, moderately dilated ileum were found plastered to the right lower quadrant at the site of the ileal fistula. The area of the fistula was found to be 3 centimeters proximal to the ileocecal valve and was associated with a stricture distal to the area of the fistula (fig. 1). The site of the stricture was grossly visible as a puckering and telescoping of the ileum into the terminal ileum 2 centimeters from the cecum. This was the area of the ileo-ileal type of intussusception and spontaneous expulsion

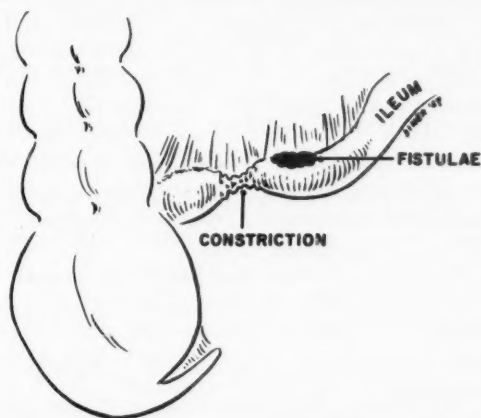


FIG. 1. Illustration of site of auto-anastomosis in terminal ileum and fistulas proximal to the stricture.

through the fecal fistula with subsequent stricture formation at the site of anastomosis. There was a very small abscess cavity into which the ileal fistula emptied before emptying onto the abdominal wall. The ileal adhesions were freed, the cecum mobilized, and the terminal 4 inches of ileum resected, including the stricture and fistula, and an end to end anastomosis was carried out, using a one-row #0000 technic. The patient had an excellent postoperative course except for slight drainage from the site of the fecal fistula, which was healed in 2 weeks. The patient had a gastric resection on April 12, 1955 at this hospital, for continued severe duodenal ulcer symptoms. At the present time he is doing well.

DISCUSSION

Benson¹ has previously commented upon the formation of a stricture at the site of auto-anastomosis of bowel. The stricture in this case was marked and prevented spontaneous closure of the fecal fistula. Resection in both of Benson's patients was necessary to establish an adequate lumen, as it was in our patient. The fistula in this case, however, worked as a release valve for the obstruction and actually prevented mandatory surgery earlier.

The stab wound must have had some relation to the cause of the intussusception, although the exact mechanism would be speculation. Transsection of a major blood vessel as in a case reported by Grant would be one mechanism. A serosal hematoma would be another possibility. Danhauser reported only 2 of the 668 collected cases of intussusception as due to stab wound and gunshot wound, which he listed together. The diagnosis of sequestration was not considered in this case until the bowel was expelled. Failure of the mass to completely disappear after the pelvic abscess was drained indicated the possibility of another intra-abdominal abscess. However, this mass subsequently proved to be the intussusception.

SUMMARY

We believe this report is the first case of expulsion of sequestered bowel through a fistula with subsequent auto-anastomosis.

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PRIMARY REPLACEMENT WITH A METALLIC INTRAMEDULLARY
PROSTHESIS IN FRESH DISPLACED FRACTURES OF THE
SURGICAL NECK OF THE FEMUR*†

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Until recently the only acceptable surgical method of treating displaced fractures of the neck of the femur has been by nailing. This method has had several drawbacks: 1. The incidence of nonunion, even with the most refined techniques, is still appreciable. 2. The incidence of delayed arthritic changes and of aseptic necrosis is very great. In Boyd's series,¹ compiled in 1947, 84.7 per cent ultimately obtained union, but only 43.6 per cent ended up with what Boyd considered good hips. Doubtless a similar series, compiled in 1957, would show better results. Nevertheless the price a patient must pay for this chance of a good result is many months of limited, if any, weight bearing. Elderly people have little time left to expend upon their hips, and have great difficulty in resuming ambulation after having been off their feet for prolonged periods.

On this account primary replacement of the head of the femur with a metallic prosthesis is becoming an increasingly acceptable procedure in elderly patients and in younger patients who are mentally incapable of following the regime that is necessary after nailing.^{4, 10, 12} This has resulted largely from the evolution of satisfactory prosthesis and the development of improved surgical approaches. The early cases done using acrylic prostheses, stabilized by a shaft perforating the lateral cortex, were not particularly gratifying. The plastics used did not hold up well, and the stem of the prosthesis tended to work loose, so that good early results were not always maintained.^{2, 4} With the development of the metallic prosthesis, having an intramedullary stem, these problems were largely solved.^{10, 13} At the present time the principal problems are how long the prosthesis and the body will tolerate one another, the technical difficulties of proper introduction, and the proper selection of patients. The realm of usefulness of the hip prosthesis is in the process of being explored.

The method of inserting the prosthesis has evolved considerably. Most of the earlier reports adhered to the Hueter incision popularized by the Judets,⁶ which approached the hip anteriorly in the interval between tensor fascia femoris and sartorius. This approach required that the hip be kept in internal rotation during convalescence lest dislocation occur, for it made a rent in the capsule anteriorly and divided the iliofemoral ligament (Bigelow's ligament). A tendency to approach the hip posteriorly developed with Gibson's,³ and later with McFarland and Osborne's,⁸ variation of the Kocher approach. As we modified it, the approach consisted of a single flap composed of vastus lateralis, capsule,

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gluteus medius and gluteus minimus, all elevated subperiosteally and in continuity. Flexion of the hip allowed this flap to be shifted forward, and external rotation delivered the fractured neck into the wound. After the prosthesis was inserted, extension of the hip repositioned the flap, which was then sutured back. Since the muscles were not divided, it was thought to be safe to ambulate these patients early, for as long as the hip was in extension, there was little strain on the suture line. Both of these approaches were, however, in the author's opinion, more formidable and more disabling for the patient than the presently used posterior approach popularized by Marcy and Fletcher⁹ and by A. T. Moore.¹⁰

Under spinal anesthesia with the patient in lateral recumbency, the broken hip uppermost and flexed, a curved incision is made through the fascia lata to expose the posterior superior portion of the trochanter. The obturator internus and gemelli are divided, a suture placed in them, and used to retract and protect the sciatic nerve. A linear incision is made in the capsule and its edges held open by retention sutures. The thigh is then internally rotated to expose the fracture site. The head is removed with a corkscrew, perhaps assisted by a Smith Petersen gouge inserted into the incisura acetabulae to break the cohesion between head and acetabulum. The head is compared with the various sizes of prosthesis available to select the proper prosthesis. The Fred Thompson vitallium prosthesis has been used routinely. The femoral heads are saved for the bone bank. It is of interest that regardless of which Pauwlen's¹¹ type the fracture has appeared to be on x-ray, the head, after removal, has appeared much the same, with a transverse fracture and a pointed spike extending downwards in back. This would support the contention of Per Linton⁷ that Pauwlen's classification is determined by the amount of displacement rather than by the mechanism of the fracture.

A suitably bent sharp $\frac{1}{8}$ inch uterine curette is useful for reaming out the medullary canal to receive the prosthesis. Rongeurs are used to nibble off the neck until the base of the prosthesis fits the neck accurately. This is done with considerable care, removing and replacing the prosthesis several times if necessary, so that the normal length of head and neck, and the normal degree of anteversion are restored. If the neck is too long, the iliofemoral ligament and capsule will be excessively taut; this will limit extension and abduction of the hip. If the neck is too short the prosthesis will not seat well upon the calcar, and the gluteus medius and minimus will be at a disadvantage. Further, the likelihood of subluxation or dislocation is considerably greater if the neck is too short and the prosthesis not impacted into the acetabulum by the pull of the musculature and capsule.

After being seated in the femur the prosthesis is reduced into the acetabulum by making traction in flexion and by pressure with the thumbs; a skid is sometimes used to prevent the interposition of soft tissues. With the anterior or anterolateral approach considerable force is often necessary to reduce the head into the acetabulum. Before we began using the posterior approach we fractured a trochanter in one patient and made a crack line in the shaft of another. It seems to us that repositioning the head is far easier with the posterior approach than



FIG. 1. A typical displaced fracture of the femoral neck in a 74 year old woman

with the anterior. With the anterior and anterolateral approaches we commonly gave one unit of blood. With the posterior approach bleeding has been so little that no transfusion has been needed except in patients with preexisting anemia. Postoperatively a position of flexion and adduction is avoided because of the incision in the posterior capsule, but the patients are up and walking as soon as they will tolerate it: this is often on the first day, particularly in those patients who have had only a short interval between fracture and replacement. We make little effort to persuade these patients to discard a cane.

This procedure has been used for 2 years at the University of Arkansas Medical Center: the cases of 23 patients, operated upon 5 or more months ago, have been reviewed. The average age was 75, with a span from 58 (a mentally retarded woman) to 92. All of these patients were indigent, most were in a poor nutritional and general medical condition, and 6 were in a state of senile dementia on admission.

The average hospital stay postoperatively was 13 days, and of the 23, 19 were ambulatory, with or without assistance, prior to discharge. There was one known death, a woman who was asymptomatic and ambulatory without assistance when she left the hospital, but who developed a pseudomonas lobar pneumonia and died 2 weeks later.

Follow-up studies were obtained on only 16; of these, 12 were excellent in that



FIG. 2. The prosthesis in position. In this case a small piece of bone has inadvertently been left behind the neck superiorly.

they have virtually asymptomatic hips and no restriction of their activities. Four were thought to be good; they have a virtually normal range of motion and no pain of which we can be sure; they are not walking as well as they were prior to their fall.

It is not thought that these figures give a true picture, however, for we have been unable to obtain a follow-up on any of the 4 patients who were not walking when they left the hospital. Of these, one had had a fracture of the greater trochanter, incurred at the time of reducing the prosthesis into the acetabulum; the remainder were severely senile.

Of the 6 patients who were classified as having "severe" senile dementia on admission, only one achieved an excellent, and 2, good results. Three could not be persuaded to walk prior to discharge and were not seen again. All of these patients had been, so far as we could ascertain, ambulatory prior to the fall which fractured their femur. Only one—the woman who died of pseudomonas pneumonia—failed to improve in general condition during the time of hospitalization on observation. The frequency of senile confusion, apparently coming on rather abruptly during the interval between their fall and their admission to the hospital would suggest that, as Howell⁵ puts it, "When an old person tumbles down for no obvious reason, the occurrence . . . is premonitory . . . and is often the herald of impending deterioration."

SUMMARY

The technic of replacing the recently fractured femoral head with a metallic prosthesis has evolved with remarkable rapidity. It is believed that a point has now been reached at which in many elderly or mentally incompetent patients primary prosthetic replacement offers a better outlook than nailing.

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EDITORIAL

THE SURGICAL APPROACH FOR ESOPHAGEAL HIATAL HERNIA REPAIR

Should the surgical repair of an esophageal hiatal hernia be performed by means of an abdominal or a thoracic approach? In observing a parade of eager debaters of this controversial point at a recent surgical meeting the author could not help but feel that an attempt was being made in some instances to "stake out a claim" rather than to reach a conclusion based on sound surgical judgement. This is, indeed, an injustice to the patient.

The exact mechanism or mechanisms involved in the sphincter action at the esophagogastric junction as well as the production of symptoms in patients with hiatal hernia remain incompletely understood. On the other hand in most surgeons' experience an Allison type of repair is largely successful in relieving symptoms and the recurrence rate is low. This repair eliminates the hernia sac, reapproximates the separated fibers of the right crus of the diaphragm posteriorly and fixes the lower esophageal segment to the inferior diaphragmatic fascia at the margin of the hiatus. These technical maneuvers can be accomplished with equal effectiveness and usually with equal ease by means of either an abdominal or a thoracic approach. It is only in the patient with the relatively rare congenitally short esophagus or with an inflammatory stricture of the lower esophageal segment that the operative approach may be of paramount importance so far as the technical aspects are concerned. These conditions demand more than a simple hernia repair and require a supradiaphragmatic operation.

Hence in the vast majority of patients the operative approach should be decided by other factors. Some of the more important are the potential operative morbidity and mortality, the probable accuracy and completeness of the preoperative diagnosis, the possibility of simultaneous surgical treatment of concomitant pathology, and postoperative sequelae. These factors must be weighed in the light of each individual patient's problems. The operation should be made to fit the patient. The "preference" of the surgeon, himself, need have little to do with the matter. Far better it be for the surgeon to be familiar with both methods so that he may apply them with equal facility, without bias, and entirely for the patient's benefit. It is absurd to champion either the abdominal or the thoracic approach to the entire exclusion of the other. The ridiculousness to which this has been carried is well exemplified by a patient recently brought to my attention who had both a sliding hiatal hernia and gallstones. After considerable argument as to which was causing the major trouble and should be surgically attacked first, the hernia was repaired transthoracically. The patient promptly obliged by developing acute cholecystitis in the postoperative period.

On the surgical service at the University of Arkansas our early experiences with this problem were limited entirely to the supradiaphragmatic approach. As more experience has been accumulated we find ourselves applying the abdominal approach increasingly. This is largely for two reasons. First, a great

number of our patients with symptoms demanding operation have fallen into the older age group, some even in the ninth decade, and have had limited cardio-pulmonary reserve. Second, a concomitant surgically remediable pathologic condition has existed within the abdomen or could not be ruled out preoperatively in clear cut fashion. The importance of the latter has at times been appreciated only at the operating table when an unsuspected lesion of some other organ completely altered the operative plans. For this reason, in utilizing the supra-diaphragmatic approach it is probably always advisable to incise the diaphragm widely enough to carry out an abdominal exploration prior to the herniorrhaphy. Otherwise a much more serious condition such as carcinoma of the stomach which was missed on preoperative roentgenograms may be entirely overlooked. That a hiatal hernia may be the "great masquerader" within the abdomen is also true in a reverse sense!

The proper approach for the repair of an esophageal hiatal hernia must be decided on an individual basis for each patient. Sound surgical judgement permits neither an abdominal nor a thoracic approach to be applied routinely. These should be considered not as competitive but as complementary methods in the armamentarium of the surgeon handling this problem.

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BOOKS RECEIVED

Books received are acknowledged in this section, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

Hypophysectomy. By O. H. PEARSON, M.D., F.A.C.P., Publisher: Charles C Thomas, Publisher.

Essentials of Modern Surgery (5th ed.). By R. M. HANDFIELD-JONES, M.C., M.S., F.R.C.S. AND SIR ARTHUR E. PARRITT, K.C.M.G., C.B.E., M.A., M.Ch., F.R.C.S. Publisher: E. & S. Livingstone Ltd.

Orthopedic Surgery in Infancy and Childhood. By ALBERT B. FERGUSON, JR., M.D., Publisher: The Williams & Wilkins Co.

Clinical Neurosurgery, Vol. 3. By CARL W. RAND, M.D., Publisher: The Williams & Wilkins Co.

1957 Medical Progress. Editor: MORRIS FISHBEIN, M.D., Publisher: McGraw-Hill Book Company, Inc.

Atlas of Eye Surgery. By R. TOWNLEY PATON, M.D., F.A.C.S. AND HERBERT M. KATZIN, M.D., F.A.C.S., Publisher: McGraw-Hill Book Company, Inc.

Surgical Management of Pulmonary Tuberculosis. By JOHN D. STEELE, M.D., Publisher: Charles C Thomas, Publisher.

Gastrointestinal Obstruction. By MEYER O. CANTOR, M.D. AND ROLAND P. REYNOLDS, M.D. Publisher: The Williams & Wilkins Co.

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